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PARTIAL THENAR ATROPHY

A CLINICAL ENTITY

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For years I have been studying a group of patients who have presented a well characterized, uniform and unchanging clinical picture. The only objective manifestation has been atrophy of the outer, radial portion of the muscles of the thenar eminence. My attention was first drawn to the problem by a patient aged 26 who presented this syndrome and whose condition was diagnosed by a neurologist as "progressive muscular atrophy." Examination of this patient and the later course of his disease proved that the disorder was not progressive muscular atrophy. My group of patients had presented diagnostic difficulties, as they were referred to the clinic with the following diagnoses: multiple sclerosis, syringomyelia, gliosis spinalis, occupational neuritis of the median nerve and neuritis of the brachial plexus.

Seven patients presented this syndrome in a clearcut form and were examined completely in the clinic or in the hospital. In addition, about 10 patients either were examined briefly or did not present an outspoken picture. Therefore, only the first 7 cases will be discussed here. Of these 7 patients, 5 were women and 2 men. The ages at the time of the first examination were 22, 26, 36, 46, 52, 53 and 55, respectively. One of the men was a worker in a sawmill, the other a rancher; of the 5 women, 2 were housemaids, 2 were housewives and 1 was without occupation.

REPORT OF CASES

The family histories were not significant. The 4 women who were housemaids or housewives had had to do much laundry and housework and to keep their hands in water a great deal. Part of the heavy work of the sawmill laborer has been to push big logs before him with the palms of his hands. In none of the 7 cases was there a history of acute or chronic poisoning or of infection of any kind.

This paper is dedicated to the memory of James Ramsay Hunt.

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Read by title at the Sixty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 5, 1939.

Five of the 7 patients had noticed first paresthesias in the tips of the fingers and palms, and 1 had also had paresthesias in the soles. These had first occurred one-half, two or six years before physicians were consulted. The paresthesias were described chiefly as a pricking sensation or as a feeling of "going to sleep" and were most pronounced in the mornings. The hands had to be rubbed to get rid of this feeling. Some of the patients complained of actual pain in the hands and arms. The paresthesias and pains occurred intermittently, lasting for months, disappearing for months and becoming worse after exertion. One patient complained that she had no "feeling in the hand;" she could not feel objects she was holding and so sometimes dropped them. In some cases the pains in the hands subsided, to be replaced by paresthesias. The paresthesias and pains were bilateral, except in 1 case in which they occurred only on the left side; on this side, one year later, the patient noticed atrophy of the thenar eminence. One patient had become aware of atrophy of his thumb a year before, and another stated that the thenar muscle had "disappeared suddenly." About half the patients did not themselves notice the atrophy; it had been called to their attention by acquaintances or by physicians.

At the time of the first examination all but 2 of the patients complained of paresthesias or pains or of a sensation of "going to sleep" in all the fingers, in the hands or, less frequently, in the soles, where they had a pricking sensation. One patient had a feeling as if his hands and feet were swollen in the evening; 1 had a "cramp" in the hands in the morning; 1 complained of a "fiery" feeling in both arms, and 1, of a feeling of coldness in the middle fingers. The paresthesias or pain did not generally favor any particular finger or the thumb. Though intermittent, the paresthesias had handicapped the patients, especially the older women, in their work.

The patients complained little of the wasting of the muscles of the thumb; some said, without particular emphasis, that their thumbs were getting thin and weak.

General Examination.—The physical constitution and state of nutrition of the patients were in general below average. None gave a history of intoxication or chronic infection of any kind. The internal organs were normal, and, except for the hands, there were no pathologic changes of significance in the nervous system. However, most of the patients were examined only in the outpatient department.

Thenar Atrophy.—The hands of the patients presented a peculiar and distinct picture that I have not observed in any other neurologic disease. The cardinal sign in all cases was a partial, sometimes sharply defined, atrophy along the radial, outer side of the thenar eminence. This atrophy cannot be described easily, but the accompanying photographs illustrate its extent and degree. In 4 cases both hands were affected; in 2 only the right, and in 1 only the left. The outer, radial part of the thenar musculature showed a striking atrophy, the muscles here having disappeared to such an extent that the outer edge of the first metacarpal bone, especially at its base, was visible and easily and distinctly palpable. The proximal end of this bone was clearly outlined. In some cases the boundaries of the atrophy were rather sharp, the inner, ulnar part of the thenar musculature showing no definite changes. The changes in this portion of the thenar eminence could, at all events, be designated as insignificant as compared with the striking changes in the outer part. From mere inspection and palpation one would assume that the muscle most involved was that which is inserted on the outer edge of the first metacarpal bone (the opponens pollicis) and, further, that the muscle that lies on

the outer part of the thenar eminence (the abductor pollicis brevis) was implicated. One had always the impression that the whole of the opponens pollicis muscle was involved, and probably also, either wholly or partially, the abductor pollicis brevis muscle. Fibrillary twitchings were never observed. The thumb approached a position in the plane of the other fingers, as seen in the flat "ape hand."

In contrast to this striking atrophy, the disturbances in function of the thumb were surprisingly slight, even in cases of bilateral involvement; at all events,

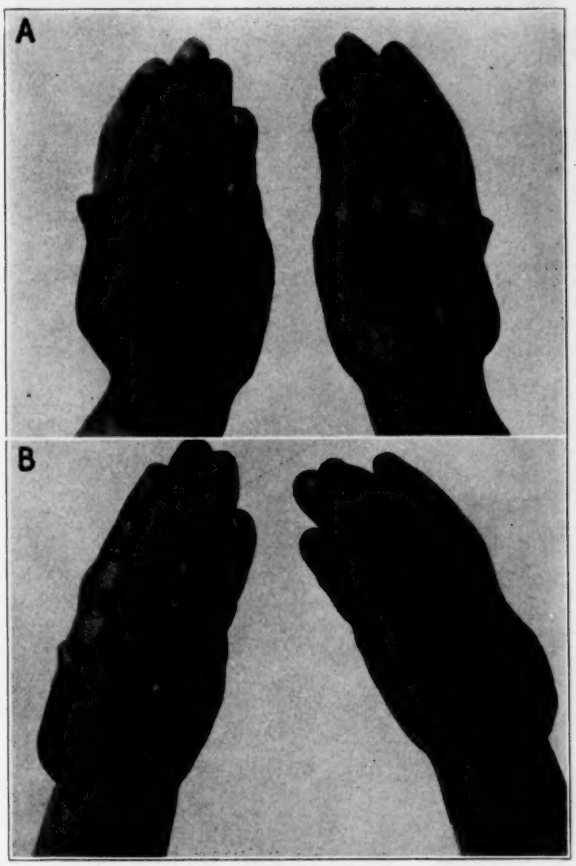

Fig. 1.—Partial thenar atrophy (*A*) on both sides in a woman aged 22 (case 1); (*B*) on both sides in a woman aged 55 (case 2).

the patients complained little of loss of function. It was the movement of opposition of the thumb which was chiefly or only affected. The ability to perform this movement, and also abduction of the thumb, was diminished, but never completely lost. In 1 case performance of opposition was good, but that of abduction poor. In the movement of opposition of the thumb, the most striking feature was that the thumb was not rotated around its axis; this movement was partially replaced by adduction and flexion.

No appreciable sensory changes in the hands, fingers or elsewhere were detected. In 1 or 2 cases the sensibility of the finger tips seemed to be impaired, and in 1 case the median nerve was tender to pressure.

Electrical examination was difficult, and interpretation of its results was not always easy. In some cases the muscles affected seemed not to react at all. In some cases there was complete reaction of degeneration in the affected muscles on

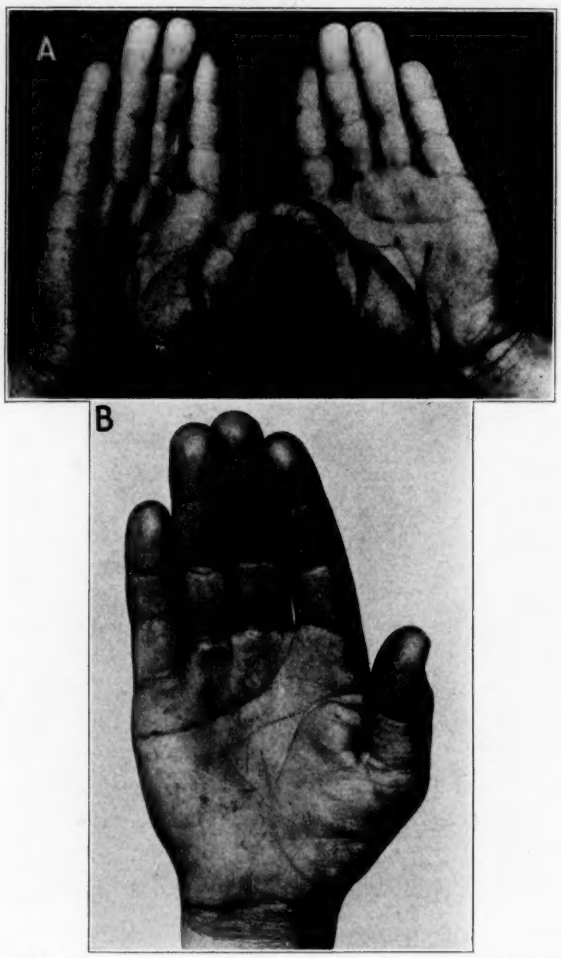

Fig. 2.—Partial thenar atrophy on the right side in a man aged 26 (case 3).

the outer part of the thenar eminence. In no case was a movement of opposition elicited by electrical stimulation.

Examination of the Spine.—Roentgenograms of the cervical portion of the spine did not in any instance reveal the presence of cervical ribs or other abnormalities; in 1 case elongation of the transverse processes of the seventh cervical vertebra was found.

Course.—Some of the patients were reexamined after two or three years, but no definite change in the atrophy was discovered—certainly, never regression, hardly progression.

Summary.—A group of 7 patients presented a more or less sharply defined and insidiously developing atrophy of the outer part of the thenar eminence on both sides or one side, unaccompanied by any other motor or sensory phenomena. Five of the patients complained of acroparesthesias of long duration.

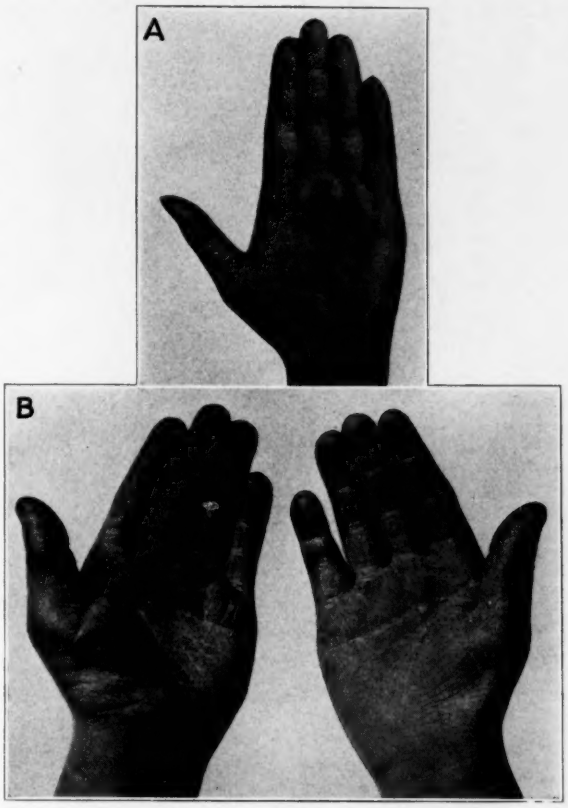

Fig. 3.—Partial thenar atrophy (*A*) on the left side in a woman aged 52 (case 4); (*B*) on both sides in a woman aged 36 (case 5).

REVIEW OF LITERATURE

The following articles in the literature contain reports of identical or more or less similar cases. Ramsay Hunt [1] described 4 cases of

1. Hunt, J. R.: (*a*) Occupation Neuritis of the Thenar Branch of the Median Nerve, Tr. Am. Neurol. A. **35**:184, 1909; (*b*) The Thenar and Hypothenar Types of Neural Atrophy of the Hand, Am. J. M. Sc. **141**:224, 1911; (*c*) The Neural Atrophy of the Muscles of the Hand Without Sensory Disturbances, Rev. Neurol. & Psychiat. **12**:137, 1914; (*d*) Thenar and Hypothenar Types of Neural Atrophy of the Hand, Brit. M. J. **2**:642, 1930; in discussion on Wartenberg,[13b] p. 254.

sharply defined muscular atrophy along the outer side of the thenar eminence. There was complete electrical reaction of degeneration in the abductor pollicis brevis and opponens pollicis muscles. No fibrillary twitchings were noted; sensation was unimpaired. In 2 of the 4 cases the atrophy was bilateral, and in 2, unilateral.

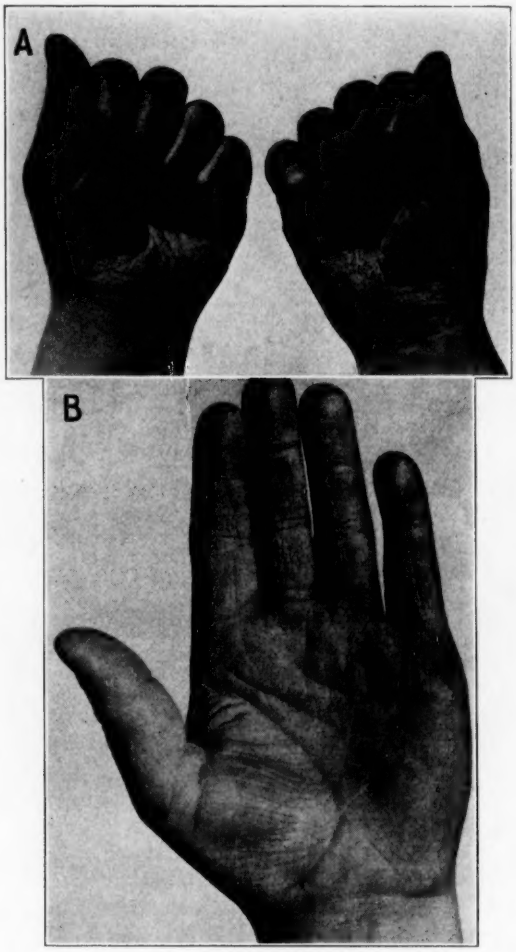

Fig. 4.—Partial thenar atrophy (case 5).

Kinnier Wilson [2] described cases of atrophy characterized by: curiously local early wasting of the muscles of the thenar eminence on the right side, in which the muscles involved were the abductor pollicis and opponens pollicis alone; all the other thenar muscles, including the flexor brevis pollicis, being intact.

2. Wilson, S. A. K.: Some Points in the Symptomatology of Cervical Rib, with Especial Reference to Muscular Wasting, Proc. Roy. Soc. Med. (Clin. Sect.) **6**:133, 1913.

Dorndorf [3] contributed a report in which were described, unfortunately without photographs, 16 cases of a similar disturbance. All of his patients were women in the period of, or after, the climacterium. The abductor pollicis brevis and opponens pollicis muscles were affected in all cases; in many instances, besides these, the superficial head of the flexor pollicis brevis muscle, and in 4 cases the deep head also, was affected. In 4 cases the adductor pollicis muscle was also involved. No disturbances in sensation were noted. The onset and later course of the disease were very slow. In most instances both hands were affected.

Zabriskie and his associates [4] reported the cases of 3 sisters with muscular atrophy affecting the thenar eminence on both sides. The photographs of the patients show atrophy corresponding in all respects

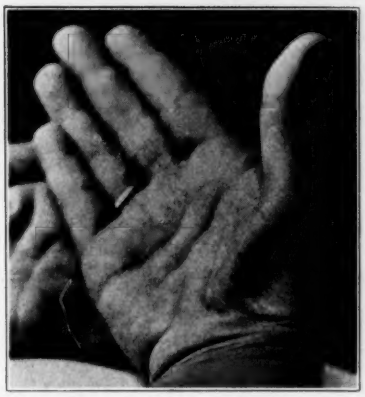

Fig. 5.—Partial thenar atrophy on the right side in a woman aged 46 (case 6).

to that of my patients. There were no muscular fibrillations or alterations in sensation.

The atrophy appeared to involve the abductor pollicis, opponens pollicis, and flexor pollicis brevis.

Moersch [5] reported a case of bilateral partial atrophy of the thenar eminence. The photograph of the patient shows an atrophy which in its location and extension corresponds exactly to that in my cases.

[There was] wasting of muscles on the outer . . . side of the thumb . . . Neurologic examination revealed nothing abnormal except the findings associated with the condition of the hands.

3. Dorndorf, G.: Ueber isolierte Lähmungen im Daumenballen, Monatschr. f. Psychiat. u. Neurol. **80**:331, 1931.

4. Zabriskie, E. G.; Hare, C. C., and Masselink, R. J.: Hypertrophic Arthritis of Cervical Vertebrae with Thenar Muscular Atrophy Occurring in Three Sisters, Bull. Neurol. Inst. New York **4**:207, 1935.

5. Moersch, F. P.: Median Thenar Neuritis, Proc. Staff Meet., Mayo Clin. **13**:220, 1938.

Sensation in the hands was not disturbed, and fibrillary twitchings were not observed.

Wertheim-Salomonson [6] mentioned having seen, in the Netherlands, cases of neuritis associated with gout in the form of "a symmetric amyotrophy in the outermost part of the thenar eminence (opponens pollicis muscle)." A photograph with the legend "median neuritis in gout" shows atrophy of the type that has been described in my cases.

Without referring to it in the text, Veraguth [7] presented a photograph showing "partial median neuritis" on one side which was similar to that in my cases.

In this review of the literature, reference has been omitted intentionally to cases in which the picture did not correspond exactly to that described in this paper. There were some cases (Marie and Foix,[8] Lhermitte and de Massary [9]) in which the atrophy affected the interosseus muscles also and some (Marie and Foix,[10] de Souza and Longo [11]) in which all of the thenar muscles were affected, instead of the outer part only, as occurred in my cases. From the description alone, without a photograph, it is doubtful if the case reported by Lhermitte and Nicholas [12] belongs to this group.

COMMENT

From my cases and those reported in the literature, it is justifiable to conclude that "partial thenar atrophy" is a definite clinical entity, with the following characteristics: atrophy of the muscles on the outer, radial part of the thenar eminence, of slow, chronic and hardly noticeable development and with a marked tendency to become stationary. No fibrillary twitchings are present. There is no tenderness of the nerve trunks, and there are no sensory changes and no other motor dis-

6. Wertheim-Salomonson, T. K. A., in Lewandowsky, M. H.: Handbuch der Neurologie, Berlin, Julius Springer, 1910-1919, vol. 2, p. 119.

7. Veraguth, O., in von Bergmann, G., and Staehelin, R.: Handbuch der inneren Medizin, ed. 2, Berlin, Julius Springer, 1926, vol. 5, pt. 1, p. 1012.

8. Marie, P., and Foix, C.: L'atrophie isolée non progressive des petits muscles de la main, Nouv. iconog. de la Salpêtrière **25**:353 and 427, 1912.

9. Lhermitte, J., and de Massary, J.: L'amyotrophie thénarienne non évolutive du vieillard, Rev. neurol. **1**:1202, 1930.

10. Marie, P., and Foix, C.: Atrophie isolée de l'eminence thénar d'origine névritique: Rôle du ligament annulaire antérieur du carpe dans la pathogénie de la lésion, Rev. neurol. **21**:647, 1913.

11. de Souza, N., and Longo, P. W.: Atrophia circumscripta aos musculos da eminencia thenar como manifestação inicial e residual da lepra, Rev. brasil. de leprol. **5**:29, 1937.

12. Lhermitte, J., and Nicholas, M.: Les amyotrophies de la main chez le vieillard, Encéphale **20**:701, 1925.

turbances. Paresthesias without, or less commonly with, pain are often present in both hands; these usually precede the appearance of the atrophy.

This clinical picture, though simple, raises highly complex diagnostic and pathogenetic problems. Previously I tried briefly to classify this disease entity and stressed the difficulty of its classification;[13] I am not yet able to give a fully satisfactory and exhaustive pathophysiologic explanation. The following may, therefore, be regarded purely as an attempt at solution of the difficult problem.

In discussing this neurologic problem, like any other, two questions must be raised. First, where is the lesion, and, second, of what kind is it? One must consider first the possibility of a disease of the spinal cord: a degenerative process or a vascular lesion.

It is easy to exclude a degenerative process, such as progressive spinal atrophy. The very slow development of the atrophy, its limitation to the muscles on the outer border of the thumb and the presence of paresthesias permit one to exclude progressive spinal atrophy of any known type.

It goes without saying that no vascular lesion in the spinal cord, regardless of its origin and localization, could produce this extremely limited and circumscribed atrophy without the occurrence of objective sensory changes and with the extremely chronic course.

The following points speak against involvement of the roots or of the brachial plexus, especially by a cervical rib or an allied condition: No cervical rib was demonstrated roentgenographically in any case, and the partial thenar atrophy was in many cases bilateral, whereas cervical rib produces chiefly unilateral signs. Clinically, the picture in this syndrome is different from that in cases of cervical rib. No case of cervical rib proved by roentgenograms has yet been reported in which there has been isolated, partial atrophy of the thenar eminence without any other signs.[14] The appearance in later life, the stationary character

13. Wartenberg, R.: (*a*) Ueber Neuritiden im Handgebiet, Abstracts, First International Neurological Congress, Berne, 1931, p. 90; (*b*) Ueber Neuritiden im Handgebiet, Proceedings of the First International Neurological Congress, Berne, 1931, p. 253; (*c*) Deutsche Ztschr. f. Nervenh. **124**:185, 1932.

14. Rist and Hirschberg (Atrophie isolée bilatérale, des adducteurs du pouce chez le porteur d'une paire de côtes cervicales, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:440, 1928) reported the case of a man aged 28 who presented atrophy of the adductor muscles of the thumb and, roentgenologically, a pair of cervical ribs. Since the atrophy had existed from the age of 4 years and was noticed after a fall on the hands, and since there were no pathologic reflexes and no sensory, trophic or vasomotor changes, it is not probable that there was any causal connection between the cervical ribs and the atrophy limited to the adductor muscles of the thumb. The authors did not take into consideration the fact that cervical ribs are often not associated with any signs.

of the syndrome, the absence of pain (especially of radicular pain), the absence of changes in motility, except for the thenar area, and in the reflexes, the absence of sensory and vasomotor disturbances and the presence of diffuse paresthesias bilaterally all speak against involvement of the roots or of the brachial plexus, especially through a cervical rib. The muscles chiefly involved in my cases were, first, the opponens pollicis and, then, the abductor pollicis brevis. Both belong to the eighth cervical and first dorsal segments. In no case was there any definite involvement of the numerous other muscles that are supplied by these two cervical segments. Buzzard [15] showed that even in uniradicular palsies of the brachial plexus there are objective disturbances of sensibility and widespread atrophic muscular palsy, both of which were absent in my cases.

Partial thenar atrophy does not correspond to the clinical picture associated with a lesion of the median nerve when the lesion lies at the wrist or higher. Photographs of patients with median neuritis, due chiefly to lesions of the power part of the arm, show distinctly diffuse atrophy of the whole thenar eminence, in clear contradistinction to involvement solely of the radial part of the thenar muscles in my cases. Median neuritis could produce partial thenar atrophy if the ulnar nerve provided the innervation for the entire remainder of the thenar musculature—i. e., both heads of the flexor pollicis brevis muscle. Such substitution of the median by the ulnar nerve, however, has not yet been observed. Also, against involvement of the whole median nerve is the absence of neuritic signs (tenderness of the nerve trunk) and of sensory, vasomotor and trophic changes, which are always present in median neuritis.

Ramsay Hunt [1b] wrote that "the atrophy is limited to the muscles of the thenar eminence supplied by the median nerve"; this statement is in contradiction to the photograph presented by him, which shows clearly that the thenar eminence was not entirely, but only partially, affected and that, of the muscles supplied by the median nerve, the superficial head of the flexor pollicis brevis was spared, apparently completely. His photograph shows, as do mine, that only the outer, radial part of the thenar muscles—an area corresponding to the opponens pollicis and abductor pollicis brevis muscles—was involved. It was in the abductor pollicis and opponens pollicis muscles that Hunt [1b] found reactions of degeneration or no response at all. It is therefore not justifiable to speak, as Hunt [1a] did, of "occupation neuritis of the thenar branch of the median nerve," since the whole thenar branch of this nerve is not affected. When Zabriskie and his associates [4] spoke of "atrophy limited to the thenar eminence," this designation, also, was

15. Buzzard, E. F.: Uniradicular Palsies of the Brachial Plexus, Brain **25**: 299, 1902.

not correct, as their photographs show atrophy only of the outer, radial side of the thenar eminence, exactly as occurred in my cases.

It is easy to rule out an arthrogenic atrophy. Harris [16] stated:

> Extreme wasting of the opponens and abductor pollicis may be seen sometimes in arthritis of the trapezio-metacarpal joint at the root of the thumb, and reaction of degeneration will be found indicative of a motor neuritis. Pain is always a feature of these cases, referred to the outer side of the wrist, and even to the elbow, with tenderness to pressure on the dorsal side of the joint.

In none of my cases were there any signs or symptoms indicative of a local arthritic process. Roentgenograms, therefore, were not taken.

The question arises as to whether the condition may result from partial involvement of the median nerve. The ramus of the median nerve for the muscles of the thenar eminence leaves the main trunk and, in order to reach the thenar muscles, may run backward and lie on the ligamentum carpi transversum, which may be a hard resting place. Here the nerve is exposed to pressure by ordinary use of the hand. Its branches leading to the abductor pollicis brevis and opponens pollicis muscles may apparently have an unusual course and are thus exposed more often than the branch to the superficial head of the flexor pollicis brevis muscle. These branches of the median nerve are purely motor, which explains the absence of sensory disturbances.

At my request, Dr. J. B. de C. M. Saunders, professor of anatomy at the University of California Medical School, made special anatomic investigations and has allowed me to include the following report.

MUSCULAR BRANCH OF THE MEDIAN NERVE TO THE THENAR EMINENCE

In the hand the median nerve gives off its terminal branches, which are muscular, cutaneous, articular and vascular. The muscular branch supplies three muscles of the thenar eminence, the abductor pollicis brevis, the opponens pollicis and the flexor pollicis brevis (superficial head). This branch is variously described as springing from the lateral terminal division of the nerve together with the digital cutaneous branches to both sides of the thumb and to the radial side of the index finger or independently. The details of the course of this major muscular branch have not to any extent been described.

The following description of the course of this important nerve is based on examination of the right and left hands of 16 cadavers. The muscular branch was observed in all instances to arise from the volar aspect of the main trunk of the median nerve independently, although associated in varying degrees of closeness with the digital branches to the thumb and the radial side of the index finger, sufficient to distinguish a lateral terminal division of the nerve. Its point of origin was seen to lie fairly constantly beneath the middle of the transverse carpal ligament. Thereafter the nerve proceeds distally beneath the ligament to its distal border, with a lateral inclination. At this point it passes through a definite canal in the lateral attachments of the ligament to the os multangulum majus (trapezium).

16. Harris, W.: Neuritis and Neuralgia, London, Oxford University Press, 1926.

In general terms, it is important to note that hereafter the nerve is highly reflected on itself from its point of passage through the ligament to pursue a recurrent course, proximally, to its division into branches of supply to the individual muscles. The canal in the edge of the transverse carpal ligament is smooth, obviously to allow of slight movement of the nerve in the wider ranges of movement in the thumb's ambit. In this way, friction and nerve stretch are avoided.

The course and distribution of the muscular branch after its passage through the canal previously described showed side variations from specimen to specimen; inconstancies no doubt related to the more recently acquired phylogenetic characteristics of the thumb. Its course can be classified as superficial and deep according to the relation which the nerve bears to the flexor pollicis brevis muscle. Before doing so, however, it is necessary to discuss the individual branches to the muscles.

The filament to the flexor pollicis brevis muscle in all 16 specimens was given off bilaterally at the medial (ulnar) border of the muscle, immediately after passage of the nerve through the fibrous canal. This filament invariably entered the deep surface of the muscle, being well protected by its fleshy substance. In 13 instances (bilaterally) the nerve to the abductor pollicis brevis and opponens pollicis muscles existed in the form of a single trunk until it reached the lateral (radial) border of the flexor pollicis brevis muscle, where it divided into individual branches for the abductor pollicis brevis and the opponens pollicis muscle. In 3 instances (bilaterally) the nerves to the abductor and opponens muscles were separated from one another, pursuing individual courses to their muscles of supply. In 1 of these cases the separate nerves ran side by side, superficial to the origin of the short flexor muscle, to their point of divergence at the lateral border of this muscle. The nerve to the abductor pollicis brevis lay distal to that to the opponens pollicis muscle. In the other 2 instances (bilaterally) the nerve to the opponens muscle passed deep to the short flexor muscle, while that to the abductor muscle coursed superficial to the flexor muscle.

The course of the nerve to the abductor pollicis brevis and to the opponens pollicis muscle can be classified as superficial, intermediate and deep according to the relation to the flexor pollicis brevis muscle. In the deep type the nerve passed beneath the flexor pollicis brevis, wholly covered and protected by the substance of this muscle. Of this type there were 6 bilateral examples. In the intermediate type, the nerve passed through the fleshy substance or the tendon of the flexor pollicis brevis muscle. The exact depth was variable. In some instances only a few fibers of the muscle covered the nerve, the remaining course being superficial; in others an appreciable amount of muscle intervened between the nerve and the surface. Of these, there were 1 unilateral and 4 bilateral examples, which included a single bilateral example in which the nerve to the abductor muscle was separate from that to the opponens muscle. In the superficial type the nerve lay superficial to the origin of the flexor pollicis brevis muscle. There were 1 unilateral and 5 bilateral examples of this type, which included 2 bilateral instances in which the nerve to the abductor muscle was separated from that to the opponens muscle. In 1 of the cases in which there were separate nerves both branches were superficial. Not in all instances of the superficial type was the nerve covered by integuments and fascia only. This depends entirely on the degree of development and extent of origin of the abductor pollicis brevis muscle. When the origin of this muscle extends along the transverse carpal ligament more distally, the flexor pollicis brevis muscle is overlapped by it, and the nerve, though superficial to the flexor pollicis brevis, is covered and well protected by the fleshy mass of the abductor pollicis brevis. In the minority, therefore, of cases of the superficial type the nerve was subcutaneous.

That rarer variations occur is indicated by a case reported by Winckler [17] in which a muscular branch was given off by the median nerve in the carpal tunnel. This filament pierced the transverse carpal ligament on its radial side, about 1 cm. from its distal border, and was directed transversely. It appeared between the superficial and the intermediate bundle of the opponens pollicis muscle, to end in the proximal portion of the latter.

In summary, it is clear that the distribution of the muscular branches of the thenar eminence is extremely variable. In general, the nerve pursues a highly reflected, or recurrent, course from its origin beneath the transverse carpal ligament. The nerve to the abductor pollicis brevis muscle may run an entirely separate course from that to the opponens pollicis muscle. In some instances the nerve of supply to both the abductor pollicis brevis and the opponens pollicis muscle, or the nerve to the abductor pollicis brevis muscle alone, may occupy for a part of its course an unprotected position just beneath the skin, where it would be liable to trauma.

The investigations by Dr. Saunders provide a new scientific basis for the assumption that the thenar branches of the median nerve may lie so unfavorably in a normal person as to be subject to trauma by the ordinary use of the hand. They lend support to the hypothesis of the neurogenic origin of partial thenar atrophy, explaining it as due to compression neuritis of the branches of the median nerve.

This is practically the same explanation of the thenar atrophy as that given by Hunt,[1b] Marie and Foix [10] and Moersch.[5] Hunt expressed the opinion that this syndrome is the "result of compression of the thenar branch of the median nerve as it emerges from beneath the annular ligament of the wrist." Marie and Foix [10] attributed the thenar atrophy in their case to interstitial neuritis located at the level of the annular ligament, with strangulation of the nerve. They considered the possibility of arresting the development of the disease by cutting the annular ligament. Moersch [5] stated:

It is likely that the thenar branch, as it emerges under the annular ligament and then swings backward and outward to the muscles, is compressed either by direct trauma or by continued irritation. . . . In the early stages of development of the atrophy, relief may be obtained by removal of irritating factors or by surgical measures, such as relieving pressure on the thenar branch of the median nerve by section of the anterior annular ligament.

Hunt called the condition "occupation neuritis of the thenar branch of the median nerve." I believe that it is hardly justifiable to speak of this disease as occupational. First, real occupational neuritis of the median nerve, due to pressure of tools on the palm, which has been described as occurring in cabinet makers, locksmiths, dentists, tailors and carpet beaters, and especially in women laundry ironers, presents

17. Winckler, G.: La branche thénarienne du nerf médian; Sa distribution et son acheminement: Etude d'anatomie comparée et d'adaptation, Arch. d'anat., d'histol. et d'embryol. **12**:151, 1930.

such a different, distinct clinical picture that it does not come into consideration for differential diagnosis. In the real occupational condition there is classic neuritis of the median nerve, with all its attributes and with or without participation of the ulnar nerve.[18] Second, in none of my cases, except possibly 1, had the occupation been such as to cause any special pressure on the volar surface of the hand and wrist. In 4 of the 7 cases both hands were involved symmetrically, the right no more than the left. In 1 case no manual work had been done, and in others the work—usual housework—did not exceed a normal amount. Zabriskie and his associates [4] stated of their cases:

> A history of any occupation which might require excessive use of certain hand muscles was not obtained in these patients.

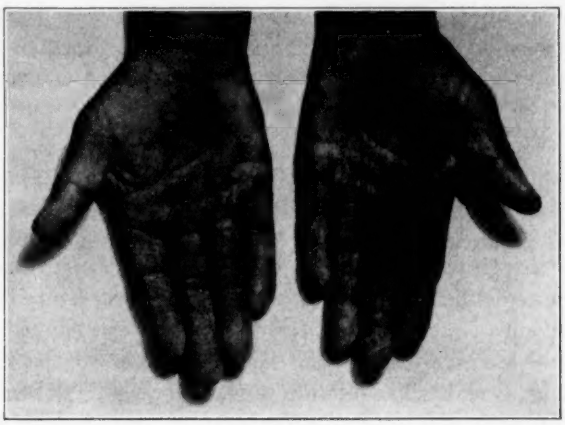

Fig. 6.—Occupational pressure neuritis of the right median nerve.

Dorndorf [3] came to the conclusion that the etiologic factors in the disease must be sought elsewhere than in damage through highly specialized overwork.

Since in no case were there any external causes, since the affected muscles had not been exposed to unusual pressure, and since millions of men traumatize their wrists and hands daily and yet thenar atrophy is an extremely rare disease, one would have to assume in the individual person an abnormal course of the nerve branches to the

18. I have just observed such a case of occupational neuritis of the median nerve in a man aged 55. This was due to pressure from the handle of heavy scissors used in pruning trees. The point of maximal pressure on the palm was at the root of the thenar muscles, in the proximal part of the palm. The clinical picture, which was diagnostically unmistakable, consisted of diffuse atrophy of the thenar musculature and hyperesthesias in the area of the median nerve, with paresthesias which occurred spontaneously and on tapping or stretching the median nerve (fig. 6).

affected muscles that allows them to be exposed to the trauma associated with normal use of the hand. One would have to assume, further, that it is principally the nerve branches to the opponens pollicis and abductor pollicis brevis muscles that are located unfavorably.

Thus, the explanation of this peculiar clinical picture might be as follows: In certain persons the nerve branches to the opponens pollicis and abductor pollicis brevis muscles are located so unfavorably in relation to the hard ligamentum transversum that normal use of the hand causes pressure on and stretching of the nerves, which leads to atrophy of these muscles alone.

One point, completely ignored by Hunt and others, complicates the subject considerably—i. e., the paresthesias of which most of my patients complained. The hands were chiefly affected. In the cases of partial thenar atrophy which have been described by other authors the patients also complained of paresthesias. Hunt,[1b] referring to his second patient, wrote:

> At the time of the onset of the atrophy, he had a numb feeling in the extreme tips of all fingers of both hands. This, however, was not permanent, and would come and go. It was not confined to the median distribution and was more in the nature of an acro-paresthesia.

Concerning his first patient, Hunt stated:

> Occasionally, during the last nine years, after an unusual stress or work, he has experienced a general numb, tired feeling in the arms and shoulders, and at times the fingers felt numb and would tingle.

Zabriskie and his associates [4] stated:

> In the cases here reported the sensation of tingling in the finger tips suggests that more than the thenar nerve is affected, even though there are no objective sensory changes.

In their first case they stated:

> Numbness and tingling had occurred in the fingers of both hands during the preceding eighteen years.

The complaints of the second patient "consisted of numbness and tingling in the finger tips of both hands of five years' duration." In the third case, the authors reported:

> Intermittent numbness and tingling in the fingers of both hands had been complained of during the previous year.

Dorndorf [8] stated that almost all his 16 patients with isolated palsies of the thenar eminence complained of paresthesias that affected diffusely the hands and arms, and eventually other parts of the body. In some cases the paresthesias were described as "severe." In some the arms

and legs were affected. The paresthesias were never limited to the area of one nerve or of one segment, and they lasted for years.

In reviewing the history and findings in all the cases, one can see that paresthesias play such an important role in the clinical picture that they should not be disregarded completely, particularly since in some cases the paresthesias preceded the atrophy by several years.

The paresthesias alone can hardly be considered responsible for the atrophy, because paresthesias are common and atrophy is rare. The most severe acroparesthesias of longest duration are not able to produce muscular atrophy. Another factor must be combined with the paresthesias to bring about this atrophy, and this factor may be the unfavorable situation of the branches of the median nerve in some persons, such as has already been described. It is usual for more than one factor to be involved in the production of a pathologic condition. Often several factors are combined. Thus, the partial thenar atrophy may develop as follows: Primarily acroparesthesias, especially in the hands and fingers, appear, which in the end are the expression of sensory polyneuritis. "Paresthesia," wrote Dana,[19] "is usually peripheral and neuritic; it means in many cases a low grade of neuritis." According to Harris,[16] some of the acroparesthesias may represent a slight degree of multiple neuritis. The fact that in my patients with paresthesias no other organic signs or symptoms have developed points to origin of these paresthesias in the periphery rather than in the cerebrum or spinal cord.

The acroparesthesias present in patients with this type of atrophy are of common occurrence and may be due to a chronic infection, intoxication or autointoxication, which in itself may remain obscure. In the light of recent investigations, one would think also of avitaminosis as a possible factor. These chronic acroparesthesias, by their very existence, give evidence of damage sustained by the peripheral nerves, even if one cannot prove it objectively by the crude methods of examination available. However, the pathologic process underlying these paresthesias cannot serve as an explanation of the thenar atrophy, because so many persons have acroparesthesias and so few have atrophy of the thenar eminence. However, if in the case of a person who had suffered for some time from paresthesias of the hands the branches of the median nerve happened to lie in the anomalous position already described, thus exposed to trauma and susceptible to other pathologic processes, such a person might be a subject for partial thenar atrophy. The branches of the median nerve would be the weakest part of his peripheral motor nervous system. It has long been my opinion, based on

19. Dana, C. L.: Text-Book of Nervous Diseases, ed. 10, New York, William Wood & Company, 1925.

study of pathologic processes of various kinds, that, generally speaking, the parts and localized areas of the central and peripheral nervous systems that are subject to chronic pressure are particularly susceptible to any pathologic process affecting the nervous system as a whole (pathoclisis).

On the other hand, it is not certain whether this anomaly of the thenar branches alone, even over a long period, could produce the thenar atrophy. This possibility is suggested by the few cases in which no paresthesias were present. It appears that, usually, the rare coincidence of two factors would be necessary for production of this disease: an abnormal course of the thenar branches of the median nerve together with general damage to the nerves in the periphery, as indicated by the presence of the paresthesias.

Thus, partial thenar atrophy belongs to the group of neuritides which Oppenheim called "toxicotraumatic," in which two factors are at work: (1) local trauma and (2) a general toxin. One might assume that in my cases the paresthesias were due to a sensory polyneuritis which, when it affects branches of the median nerve that are abnormally located and hence subject to trauma, brings about atrophy of the muscles supplied by these branches.

It is noteworthy that in typical polyneuritis partial thenar atrophy apparently does not occur. This may be due to the fact that the abnormal course of the branches of the median nerve that is necessary to bring about this atrophy is rare, and also that in acute motor polyneuritis the pathologic process affects markedly all the peripheral nerves and muscles and therefore the preferential involvement of the radial part of the thenar eminence is not noticeable, or perhaps, though present, has not been noted. From the marked atrophy in my cases one must conclude that the abnormally located branches of the median nerve have a markedly increased susceptibility and that the range of difference between their susceptibility and that of the other peripheral nerves must be great.

In submitting this toxicotraumatic hypothesis to criticism, one must consider its two components: (1) that the nerves to the outer part of the thenar eminence have been subject to an unknown damaging influence, which has also produced the acroparesthesias, and (2) that these nerves have been exposed to mechanical trauma by ordinary use of the hand. The question now arises as to whether the combination of these two factors would be capable of producing such a marked muscular atrophy.

In partial thenar atrophy the influence of the pathologic process underlying the acroparesthesias cannot be strong, as it has not been able —though in many cases it had existed for years—to produce changes elsewhere in the peripheral nervous system, such as would be evidenced by muscular, reflex or sensory changes or by ataxia.

Therefore, more effective and stronger must be the role played by the second factor, i. e., the unfavorable superficial situation of certain branches of the median nerve. It is open to question whether this anomaly can be the principal cause of the atrophy. The following points may be brought against it:

1. Such complete atrophy of muscles due to a variation in the position of their nerves in relation to a ligament would be an unparalleled neurologic occurrence. Variation in the course of the nerves occurs often. Many nerves lie superficially either on or on the edge of a ligament; and yet no other type of complete muscular atrophy due to normal use of a normal extremity is familiar. Whether nerves, such as the ulnar or the peroneal, which lie directly on a bone, may, by this very location, become completely functionless under otherwise normal conditions is questionable.

2. The partial thenar atrophy, as seen in my cases and as described by Dorndorf, Zabriskie and his associates and Moersch, appears more commonly in the later decades of life—i. e., not during the period of the greatest use of the hands.

3. The course of the atrophic process seems to be much too slow for compression neuritis. In compression neuritis the period of latency of the disease may be long, but once the process has begun the development is usually much more rapid.

4. Even if purely motor nerve branches have been compressed or strangulated at one point, the complete absence of any local "tender point" (Browning [20]) or other sensory phenomena, even transient, in the highly sensitive palm would be remarkable in compression neuritis.

5. It is further remarkable that in cases of bilateral involvement there is nearly complete symmetry of the atrophy. The atrophy is of equal degree on both sides, and is not greater in the right hand, which is certainly used much more than the left by right-handed persons. Nor is there in the histories of the patients any indication that the atrophy began on the right side. In 1 of my cases—that of a right-handed person—only the left side was involved, which could not be explained on an occupational basis.

6. As far as can be judged from the literature, real occupational neuritis of the median nerve due to the pressure of tools on the palm does not start with atrophy limited to the outer side of the thenar eminence. The transition of partial thenar atrophy into fully developed occupational neuritis of the median nerve has apparently never been observed.

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20. Browning, W.: The Tender Point in Pressure-Paralysis of Peripheral Nerves, Kansas City M. Index-Lancet **22**:197, 1901.

7. Dorndof pointed out that in none of his cases was improvement of the atrophy observed, despite intensive electrical treatment. Neither have my patients shown the least improvement.

From all this, the conclusion is justifiable that the toxicotraumatic hypothesis cannot offer conclusive evidence that the partial thenar atrophy is a neurogenic disorder. It may, but it need not, have such an origin.

In looking for a possible location of a lesion which might lead to partial thenar atrophy, I have followed in succession all the portions of the lower neuron, from the spinal cord to the branches of the median nerve for the muscles affected. It remains now to discuss whether a purely muscular disturbance can be responsible for the disease. Such a disorder might be either exogenous or endogenous.

An exogenous lesion can arise practically only from overuse or from direct pressure on the muscles in occupational use. Teleky [21] described the case of a file cutter aged 41 with complete atrophy of the lower parts of the abductor pollicis brevis and opponens pollicis muscles of the right hand. He ascribed the atrophy to occupational overuse of these muscles. Such an etiologic factor does not come into consideration in my cases, as in no instance was the occupation such as to bring about special overuse of these muscles.

As an endogenous disease, the only condition that comes into consideration would be an autochthonous muscular degeneration, an abiotrophy in the sense of Gowers ("deficient development," Mariana; "congenital inferiority," Oppenheim). This is due to a defect in development of some muscle or muscle groups which may become evident in later years. The so-called *infantiler Kernschwund,* of Moebius, affecting the nuclei of the ocular muscles, offers a neurologic analogy to this muscular degeneration. This *Kernschwund,* a typical autochthonous disease, may make its appearance as late as the fifth decade of life.

In comparing this hypothesis of muscular heredodegeneration with that of compression neuritis of the median nerve, the following points may be raised in favor of the former hypothesis:

1. The thenar musculature, especially the opponens pollicis, in man is phylogenetically a recent acquisition. This muscle was chiefly and most profoundly involved in all my cases, and next to this was the abductor pollicis brevis. Like all other phylogenetically young structures, these muscles are subject to malformations, aplasias and hypoplasias, as they represent, so to say, the weakest point of the neuromuscular axis. In connection with my cases, one reported by Kramer [22]

21. Teleky, L.: Isolierte Atrophie einzelner Daumenballenmuskeln bei Feilhauern, Wien. klin. Wchnschr. **26**:374, 1913.

22. Kramer: Kongenitaler Muskeldefekt, Zentralbl. f. d. ges. Neurol. u. Psychiat. **40**:375, 1925.

is of importance. The patient had had since birth a defect in the thenar musculature bilaterally. The abductor pollicis brevis and opponens pollicis muscles were entirely absent; the abductor pollicis was preserved, and also the flexor pollicis brevis to considerable degree, even in the portion innervated by the median nerve. In this patient the same muscles as were essentially involved in my cases showed congenital aplasia. In my cases a congenital deficient development could have produced late and prolonged degeneration of the muscles.

2. There is apparent absence (as already discussed) of an adequate external cause for the marked muscular atrophy.

3. There is bilateral symmetry of the muscular involvement which, by the way, is often seen in other congenital muscular defects of the arms and hands. I have seen a case of complete bilaterally symmetric absence of the abductor pollicis longus muscle.

4. There is predominance of the atrophy over the paralysis, whereas in a neuritic disorder one would expect the opposite to occur.

5. The course is extremely slow and hardly noticeable.

6. There is complete absence of any local sensory phenomenon whatever.

7. The condition appears in the later decades of life.

8. A hereditary factor was shown in the cases of 3 sisters who were affected, as reported by Zabriskie and his associates.[4]

However, in consideration of this hypothesis, as in discussion of the neurogenic origin, the question of the influence and importance of the acroparesthesias arises. Assuming that the atrophy is due to an abiotrophy—a congenital inferiority of the phylogenetically young muscles—how could this endogenous factor be combined with acroparesthesias? Two answers merit consideration: First, the combination may be accidental, since acroparesthesias are common. In 2 of my cases and in some of those reported in the literature there apparently were no acroparesthesias. However, this answer is hardly satisfactory because, as has been shown before, the acroparesthesias play too great a role to be neglected in consideration.

Second, two factors may occur in combination, as was discussed in connection with the possible combination of the acroparesthesias and the unfavorable position of the branches of the median nerve. One might assume that in some persons the muscles on the outer part of the thenar eminence are congenitally inferior and degenerate spontaneously but that this is more likely to occur if, in addition, the nerves of these muscles are subject to a damaging influence, such as that evidenced by the acroparesthesias. One knows that the clinical appearance and development of congenital defects may sometimes be influenced and precipitated by external causes.

Though the last hypothesis seems to be more convincing, there is at present no compelling evidence that would lead to its acceptance. Only further investigations, especially pathologic studies, can make possible a decision. These investigations should include the study of the role, if any, of the paresthesias in producing this clinical picture. Such studies would be not only of theoretic interest but also of practical importance in the treatment of these patients.

At all events, partial thenar atrophy deserves to have a definite place as a clinical entity in neurologic diseases.

SUMMARY

Several cases are described in which there occurred slowly developing, partial muscular atrophy, limited to the muscles on the outer, radial side of the thenar eminence. The atrophy probably involved only the abductor pollicis and opponens pollicis brevis muscles. There were no other pathologic findings, but most of the patients complained of paresthesias of long duration, especially in the hands and the fingers.

An attempt has been made to explain this "partial thenar atrophy," which may be regarded as a clinical entity, on the basis of toxicotraumatic damage of the corresponding branches of the median nerves. The presence of a toxic influence on these nerves is indicated by the paresthesias, which may be considered as an expression of chronic sensory polyneuritis due to an undetermined endotoxic or exotoxic process. The traumatic factor is supplied by the fact that in some persons the branches of the median nerve to the muscles of the thenar eminence may have an abnormal course in relation to the ligamentum carpi transversum, and this be subjected to abnormal pressure, stretching or strangulation in ordinary use of the hand. These two factors would need to coincide in order to produce the partial thenar atrophy, and this would account for the relative rarity of the condition.

The second possible explanation, which seems to be more convincing, is based on the assumption that the muscles involved, because they are phylogenetically young structures, may be congenitally inferior and therefore may become abiotrophic and degenerate during the course of life. This degeneration may take place spontaneously, but it may also be precipitated by added external damage, such as the pathologic condition that underlies the acroparesthesias.

NOTE.—Since this paper was written, I have read an article by Dr. B. Brouwer,[23] in the second part of which, entitled "Biological Reflections on Neuritis of the Medianus," he described cases, illustrated with photographs, of "isolated degeneration of the opponens

23. Brouwer, B.: The Significance of Phylogenetic and Ontogenetic Studies for the Neuropathologist, J. Nerv. & Ment. Dis. **51**:113, 1920.

pollicis and the abductor pollicis in neuritis of the median nerve." His cases correspond essentially with those I have described. Brouwer did not mention the work of Ramsay Hunt and others, and the similarity of his cases to those described by Hunt had apparently escaped him. Furthermore, his article has escaped the attention of all who have since written on this subject. His views on the pathogenesis of the condition corresponds to the second hypothesis presented in this paper. Having discussed the phylogenesis of the small radial muscles of the hand, Brouwer said:

> Reviewing these facts, then it is clear in what way we have to judge the great vulnerability of the opponens and the abductor policis brevis, as the clinical observations have taught us. The finer construction of the thumb and the higher functional significance, which it has received in the phylogenesis, is accompanied by a greater vulnerability.

Brouwer, however, still spoke of "a neuritis of the median nerve" and expressed the opinion that in some cases the "cause" of the condition might be hyperfunction of the muscles, as in tailors, cigar markers and housewives who do much laundry, or arthritis. In some cases, however, "no cause could be found for the alteration." Differing somewhat with Brouwer, I prefer not to speak of neuritis and wish to lay more stress on the fundamental importance of the inherent abiotrophy of the two muscles of the hand that are involved. Though the partial thenar atrophy may be precipitated by external causes, this constitutional abiotrophy is the primary factor and by itself can produce a pathologic condition of the hands.

EXPERIMENTAL STUDY OF PATHOGENESIS OF CEREBRAL CHANGES FOLLOWING PROLONGED INSULIN HYPOGLYCEMIA

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In a previous communication [1] we presented the results of the chemical analyses of the brains of cats which survived severe insulin shock without treatment. Clinically, these animals presented a picture best described as that characteristic of decerebrate rigidity. The symptoms included lack of response to the environment, insensibility to painful stimuli, gross impairment of gait and increased extensor tonus of the extremities. Chemically, evidences of a marked disturbance in the distribution of water and electrolytes in the brain were demonstrated. These were interpreted as secondary to widespread cellular injury and were considered manifestations of cellular disintegration of varying degrees. This was confirmed by histopathologic examination of the involved brains,[2] which revealed widespread necrobiosis of the ganglion cells of the cortex, basal ganglia and upper part of the medulla. Histologic evidence of comparable nature demonstrating damage to the central nervous system as a result of insulin hypoglycemia in animals,[3] as well as in man,[4] has also been described by other investigators.

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1. Yannet, H.: The Effect of Prolonged Insulin Hypoglycemia on Distribution of Water and Electrolytes in Brain and Muscle, Arch. Neurol. & Psychiat. **42**:237 (Aug.) 1937.

2. Zimmerman, H. M., and Yannett, H.: The Histopathology of the Cerebral Changes Following Prolonged Insulin Hypoglycemia, to be published.

3. (*a*) Stief, F., and Tokay, L.: Beiträge zur Histopathologie der experimentellen Insulinvergiftung, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:434, 1932; (*b*) Weitere experimentelle Untersuchungen über die cerebrale Wirkung des Insulins, ibid. **153**:561, 1935. (*c*) Grayzel, D. M.: Changes in the Central Nervous System Resulting from Convulsions Due to Hyperinsulinism, Arch. Int. Med. **54**:694 (Nov.) 1934. (*d*) Schereschewsky, N. A.; Mogilnitzky, B. H., and Gorjaewa, A. W.: Zur Pathologie und pathologischen Anatomie der Insulinvergiftung, Endokrinologie **5**:204, 1929. (*e*) Weil, A.; Liebert, E., and Heilbrunn, G.: Histopathologic Changes in the Brain in Experimental Hyperinsulinism, Arch. Neurol. & Psychiat. **39**:467 (March) 1938.

4. Bowen, B. D., and Beck, G.: Insulin Hypoglycemia, Ann. Int. Med. **6**:1412, 1933. de Morsier, G., and Mozer, J. J.: Lésions cérébrales mortelles par hypo-

(Footnote continued on next page)

The present extensive employment of insulin shock as a therapeutic agent in the treatment of psychotic disorders has brought this evidence of insulin toxicity into increasing prominence. It was believed that a more adequate conception of the etiologic factors that may be responsible for the cerebral damage following administration of insulin may lead to a better understanding of the indications and limitations of this potentially dangerous therapeutic procedure.

It may be pertinent briefly to summarize the factors that have been suggested and may be considered as possible etiologic mechanisms in the production of cerebral injury following severe insulin hypoglycemia.

1. Insulin hypoglycemia, with its associated convulsive phenomena, either through interfering with the respiratory exchange of gases or by other means, may produce cerebral anoxemia. With large doses of insulin this state may persist long enough eventually to produce cerebral damage.

2. During the later stages of insulin hypoglycemia, the general picture associated with the hypothermia has suggested the presence of marked circulatory collapse, with associated impairment of cerebral circulation.

3. Since the brain utilizes dextrose almost exclusively for its metabolic needs, prolonged periods of hypoglycemia may lead to what may be called, for want of a more suitable term, cellular starvation. This may lead to irreversible cellular changes if present over a long enough period.

4. Insulin, aside from its hypoglycemia-producing effect, may have a direct injurious action on the brain under certain conditions.

The purpose of the present paper is to present a summary of the results of our investigations on these possible etiologic factors.

GENERAL PROCEDURE AND METHODS

Cats weighing from 2 to 3.5 Kg. were used as the experimental animals. They were maintained for at least one week on an adequate diet of canned fish and milk before being studied. The last feeding took place twenty-four hours before the experiments were begun. Pentobarbital sodium was used as the anesthetic. This was injected intraperitoneally in an initial dose of 30 mg. per kilogram of body weight, followed by a subcutaneous injection of 10 mg. per kilogram within four hours if necessary.

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glycémie au cours d'un traitement insulinique chez un morphinomane, Ann. de méd. **39**:474, 1936. Bodechtel, G.: Der hypoglykämische Shock und seine Wirkung auf das Zentralnervensystems, zugleich ein Beitrag zu seiner Pathogenese, Deutsches Arch. f. klin. Med. **175**:188, 1933. Moersch, F. P., and Kernohan, J. W.: Hypoglycemia: Neurologic and Neuropathologic Studies, Arch. Neurol. & Psychiat. **39**: 242 (Feb.) 1938.

Oxygen saturation of arterial blood was determined by the method of Van Slyke and Neill.[5]

Blood sugar was determined by Folin's ferricyanide colorimetric method.[6] The blood filtrate was prepared by precipitation with zinc sulfate and sodium hydroxide. By this method the so-called true blood sugar may be determined. With the quantities of blood employed for the individual determinations, the method has a high degree of accuracy at levels above 20 mg. per hundred cubic centimeters. Below this level the sensitivity of the method diminishes, so that values less than 10 mg. per hundred cubic centimeters must be considered only as close approximations.

The insulin[7] was injected subcutaneously.

Since the nature of the various experiments differed, the specific procedures will be described with the results of the individual experiments.

RESULTS

1. *Effect of Pentobarbital Sodium on Sensitivity to Insulin.*—Animals under the influence of pentobarbital sodium showed increased sensitivity to the action of insulin. Thirty-seven animals receiving from 10 to 20 units of insulin per kilogram of body weight were observed for twenty-four hours without treatment. Among these animals there was a mortality of 27 per cent (10 deaths). Twelve animals showed evidence of extensive injury to the brain, as described elsewhere.[8] When a similar dose of insulin was injected into animals previously anesthetized with pentobarbital sodium, the mortality rate after twenty-four hours was 88 per cent (14 deaths in 16 animals). The 2 remaining animals showed evidence of widespread cerebral involvement. Without pentobarbital sodium evidence of cerebral damage following insulin rarely occurred when less than 15 units per kilogram was injected and never occurred when less than 10 units of insulin per kilogram was used. With pentobarbital sodium 3 animals showed extensive cerebral damage after the injection of 5 units per kilogram.

Since the anesthetized animals passed into the hypoglycemic state without exhibiting convulsive phenomena, convulsions per se played no role as an etiologic factor in the production of the cerebral lesions observed in the experimental animals.

2. *Effect of a Large Dose of Insulin on Oxygen Saturation of Arterial Blood.*—The oxygen saturation of arterial blood was determined in 6 control animals under anesthesia induced by pentobarbital sodium for periods varying from four to eight hours and in 5 animals, under pentobarbital anesthesia, after the injection of 20 units of insulin per kilogram of body weight. The blood sugar, determined simultaneously in the animals given insulin, in all cases was less than 30 mg. per hundred cubic centimeters. The results are given in table 1. Although the average oxygen saturation of arterial blood for the control group is probably significantly higher than that for the group given insulin, the difference is too small to be considered of physiologic significance in the production of extensive cerebral damage.

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5. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523, 1924.

6. Folin, O.: Supplementary Note on the New Ferricyanide Method for Blood Sugar, J. Biol. Chem. **81**:231, 1929.

7. The insulin, in unmodified form, was furnished by Eli Lilly & Co., Indianapolis.

8. Yannet.[1] Zimmerman and Yannet.[2]

3. *Effect of a Large Dose of Insulin on Maintenance of Arterial Blood Pressure.*—A slight fall in blood pressure is occasionally seen in patients during insulin shock. It was therefore necessary to rule out the possibility that the relatively large doses of insulin used in these experiments might result in a fall in blood pressure sufficient to impair cerebral circulation and thus produce cerebral injury.

The blood pressure, with the use of a mercury manometer attached to a glass cannula containing a solution of sodium citrate and inserted in the carotid artery, was measured in 6 animals throughout the period of insulin hypoglycemia. These animals received 25 units of insulin per kilogram and were anesthetized with pentobarbital sodium in the usual manner. The blood pressures were maintained at from 100 to 130 mm. of mercury up to a few moments before death occurred from respiratory failure. The blood pressure of normal anesthetized cats under similar conditions varies at about 120 mm. In view of the maintenance of a relatively normal blood pressure throughout the period of insulin hypoglycemia, it must be considered unlikely that any marked degree of general circulatory impairment could exist and that serious impairment of cerebral circulation was responsible for the damage to the brain. Recently, Leibel and Hall [9] have described decreases of about 25 per cent in the cerebral blood flow of rabbits during the convulsive state of insulin hypoglycemia (2 units of insulin per kilogram). When convulsions did not occur, although hypoglycemia was present, no changes in cerebral blood flow could be demonstrated. In the same study, metrazol convulsions were also found to reduce cerebral blood flow. It seems that the convulsions per se, rather than the hypoglycemic state, were responsible for the impairment of cerebral circulation. It should be pointed out in this connection that the cerebral changes we have demonstrated after insulin hypoglycemia were also produced in animals given injections of insulin while under anesthesia and therefore not exhibiting convulsions. Moreover, that the convulsions themselves played no etiologic role can be shown by the fact that with smaller doses of insulin cerebral damage could not be demonstrated even though the animals exhibited prolonged convulsive seizures.

TABLE 1.—*Effect of Hyperinsulinism on Oxygen Saturation of Arterial Blood*

Normal				After Insulin			
Animal No.	Period of Anesthesia, Hr.	Arterial Oxygen Saturation, %	Arterial Blood Sugar, Mg. per 100 Cc.	Animal No.	Period Before Death, Hr.	Arterial Oxygen Saturation, %	Arterial Blood Sugar, Mg. per 100 Cc.
1	4	97.4	113	1	1	86.6	0
	6	96.4	148	2	6	85.3	3
2	1	97.6	...		4	85.7	0
	3	91.1	160	3	6	91.2	28
	6	86.1	172	4	3	89.3	25
3	6	91.5	144	5	4	86.7	8
4	1	90.9	82		Average	87.5	
	6	95.6	130				
5	6	97.0	186				
6	4	86.0	152				
	Average	95.0					

4. *Relation of Size of the Insulin Dose, Length of the Period of Hypoglycemia and Eventual Outcome.*—In table 2 we have summarized the results of repeated

9. Leibel, B. S., and Hall, G. E.: Cerebral Blood Flow Changes During Insulin and Metrazol Shock, Proc. Soc. Exper. Biol. & Med. **38**:894, 1938.

analyses of arterial blood sugar in 15 animals given injections of insulin in graded doses. The blood was examined approximately every two hours until a normal blood sugar level was maintained or the animal succumbed. The animals were all anesthetized with pentobarbital sodium in the usual manner. The dose of insulin varied from 3 to 20 units per kilogram of body weight. In the table the period of hypoglycemia represents the interval during which the blood sugar concentration was 20 mg. per hundred cubic centimeters or less. The presence or absence of cerebral changes was determined by chemical and histologic examination. In every animal the blood sugar concentration reached hypoglycemic levels within from thirty to sixty minutes after the injection of insulin. During the period of hypoglycemia the sugar concentrations varied between 0 and 20 mg. per hundred cubic centimeters, the values being irregularly distributed and not related to the size of the dose of insulin.

Of the 9 animals receiving 8 units per kilogram or more only 1 recovered. The animal was hypoglycemic for six hours after the injection of 10 units per kilogram. Six animals died after periods of hypoglycemia varying from six to

TABLE 2.—*Relation of the Size of the Dose of Insulin and the Length of the Period of Hypoglycemia to the Clinical Outcome*

Animal No.	Dose of Insulin, Units per Kg.	Period of Hypoglycemia, Hr.	Results	Animal No.	Dose of Insulin, Units per Kg.	Period of Hypoglycemia, Hr.	Results
1	20	10	Survived, with cerebral damage	9	8	10	Survived, with cerebral damage
2	20	6	Died	10	5	12	Survived, with cerebral damage
3	20	10	Died				
4	18	12	Died	11	5	12	Recovered
5	10	6	Died	12	5	8	Recovered
6	10	6	Recovered	13	5	15	Recovered
7	10	6	Died	14	3	6	Recovered
8	8	10	Died	15	3	12	Recovered

twelve hours, and 2 animals survived, the brain showing extensive damage when examined the following day, after ten hours of hypoglycemia. Of the 6 animals that received 5 units per kilogram or less, all recovered completely except 1, which showed evidence of injury to the brain. The period of hypoglycemia in these animals varied from six to fifteen hours. It is apparent, therefore, that the degree and extent of the period of hypoglycemia cannot be directly related to the outcome in these animals. In other words, whether the animals recover, succumb or survive with evidence of injury to the brain is not primarily dependent on the period of hypoglycemia. On the other hand, recovery appeared to be the rule when the smaller doses of insulin were employed, while the serious sequelae were associated with the larger doses.

It is apparent from these experiments that the brain can safely withstand prolonged periods of hypoglycemia only when these are secondary to relatively small doses of insulin. Since the evidence of injury to the central nervous system seems to be related to the relative quantity of insulin injected, one may surmise that the injurious effects of insulin are produced primarily not by the lowering of the blood sugar but by a direct action of insulin on the brain cells.

5. *Effect of a Large Dose of Insulin When the Blood Sugar Is Maintained at a Normal Level by the Continuous Infusion of Dextrose.*—The following experiments were devised in order to determine whether the toxic effect on the central nervous system of insulin in the large doses employed in the previous experiments could

be manifested in the presence of a normal blood sugar level. Five animals were anesthetized with pentobarbital sodium as previously described and were given injections of 25 units of insulin per kilogram of body weight. After this a cannula was inserted into the femoral vein and a 5 per cent solution of dextrose allowed to infuse at such a rate that the blood sugar, determined at frequent intervals, was maintained at about 100 mg. per hundred cubic centimeters. This required from about 20 to 30 cc. per hour for animals weighing from 2 to 3 Kg. The infusion was allowed to continue about ten hours. The 5 animals that received the infusions of dextrose made complete recoveries. Histologic and chemical examinations of the brains of these animals, carried out twenty-four hours after the injection of insulin, showed no abnormalities.

It appears from these experiments that the injurious effects of the direct action of insulin on the cerebral cells are prevented by a normal concentration of blood sugar. These experiments also tend to disprove the contention that the injurious effects of insulin on the brain are related to a foreign noxious substance present in commercially prepared solutions of insulin and acting as a contaminant.

COMMENT

The brain is apparently dependent on the metabolism of carbohydrate material for its source of energy.[10] Since the reserve supply of carbohydrate in the brain, either as dextrose or as other organic compounds, is small,[11] it is the dextrose reaching the brain through the blood stream that must serve as the main source of oxidizable material. Under certain conditions lactic acid is removed from the blood passing through the brain and metabolized,[12] but as a significant source of energy this mechanism must play a relatively minor role. One may surmise, therefore, that during severe insulin hypoglycemia the cerebral cells, within a comparatively short period, are subjected to an environment in which there is little or no available source of energy. The possibility that it is the lack of available foodstuff which is responsible for the cerebral injury following large doses of insulin seems a reasonable assumption.

We have shown in this study that no significant difference in the degree of hypoglycemia or in the length of the hypoglycemic period can be demonstrated in animals given injections of small doses of insulin (i. e., 3 units per kilogram) as compared with animals given much larger doses (i. e., 15 to 20 units per kilogram). Yet after the

10. Holmes, B. E., and Holmes, E. G.: Contributions to the Study of Brain Mechanism: I. Carbohydrate Metabolism; Preliminary Report, Biochem. J. **19**: 492, 1925. Holmes, E. G., and Holmes, B. E.: Contributions to the Study of Brain Metabolism: III. Carbohydrate Metabolism; Relationship of Glycogen and Lactic Acid, ibid. **20**:1196, 1926.

11. Kerr, S. E., and Ghantus, M.: The Carbohydrate Metabolism of the Brain: II. The Effect of Varying the Carbohydrate and Insulin Supply of the Glycogen, Free Sugar and Lactic Acid in the Mammalian Brain, J. Biol. Chem. **116**:9, 1936. Holmes and Holmes.[10]

12. Himwich, H. E., and Nahum, L. M.: Respiratory Quotient of Brain, Am. J. Physiol. **90**:389, 1929. McGinty, D. A.: Regulation of Respirations: Variations in the Lactic Acid Metabolism in the Intact Brain, ibid. **88**:312, 1929.

smaller quantity of insulin the animals recovered, untreated, without cerebral involvement, while complete recovery practically never occurs after the large doses of insulin. This suggests that, aside from the hypoglycemia which they bring about by action on the liver and muscles, large doses of insulin promote certain reactions in the cerebral cells which lead to serious injury when the blood sugar remains low, but which are apparently harmless when the blood sugar is maintained at relatively normal levels by the injection of dextose.

A summary of the recent literature on the nature of the action of insulin on tissue cells in general has yielded little information that might throw light on the probable nature of the action of insulin on the brain cell. Whether this action is similar to that occurring in the muscle or liver cell must be left for future elucidation.

Because certain chemical symptoms following anoxemia resemble the hypoglycemic syndrome and because anoxemia tends to increase the likelihood of convulsions following injections of insulin,[13] it has been suggested that insulin may injure the brain cells indirectly through the production of cerebral anoxemia. The possibility that hyperinsulinism may lead to a state of relative circulatory collapse and thus adversely affect the brain has also been suggested. The work herein reported could find little support for these possibilities.

The observations of Dameshek and Myerson,[14] who showed diminution in the amount of oxygen removed from the blood passing through the brain during insulin hypoglycemia, may be explained as secondary to the deficit of metabolizable material rather than any inherent defect in the availability or utilization of oxygen. This is favored by the absence of injury to the brain following large doses of insulin when intravenous infusions of dextrose supply the necessary fuel. Such terms as "intracellular anoxemia" [3e] to designate the condition are too nebulous to contribute anything to the understanding of the problem.

The fact that pentobarbital anesthesia tends to augment the toxic action of insulin on the central nervous system might suggest a similarity in the mechanism of the action of these substances on the cerebral cell. However, this does not necessarily follow. Moreover, knowledge is equally scanty as regards the nature of the underlying mechanism of anesthesia. The peculiar relation between pentobarbital sodium and insulin, however, should be considered in the clinical use of the barbiturates for sedation during the institution of insulin therapy. Until more fully investigated, they should be considered as potentially dangerous adjuncts.

13. Glickman, N., and Gellhorn, E.: Effect of Oxygen Deficiency on the Sensitivity of Rats to Insulin, Am. J. Physiol. **121**:358, 1938.

14. Dameshek, W., and Myerson, A.: Insulin Hypoglycemia: Mechanism of the Neurologic Symptoms, Arch. Neurol. & Psychiat. **33**:1 (Jan.) 1935.

The results of this and of the previous study [1] allow certain implications concerning the therapeutic use of insulin for conditions such as the psychoses. It should be emphasized that at present there are no absolutely satisfactory means of determining how long the cerebral cells may safely be exposed to hypoglycemia produced by large doses of insulin before irreversible cerebral changes, such as are found in the experimental animals as well as in the occasional case of therapeutic fatality, manifest themselves. The degree of hypoglycemia, the length of the hypoglycemic period and the clinical picture during hypoglycemia are not adequate measuring rods in this respect. The factors responsible for the inherent variability in the response of the animals, as well as that of human subjects, are at present inadequately understood. As long as these factors remain unknown, the therapeutic use of large doses of insulin for the production of hypoglycemic shock will remain a procedure involving considerable danger. In the case of institutionalized patients with psychoses of long standing for whom the outlook is relatively hopeless, the risk involved in a procedure holding out any conceivable hope of amelioration may not be a serious deterrent to its use. However, the institution of this type of therapy in cases in which diagnosis has followed a relatively short period of observation should be deprecated. The potential danger of producing irreparable damage to the brain in some patients who might be expected to have spontaneous and lasting remissions under the more conservative forms of therapy should be seriously considered.

SUMMARY

The present study is an investigation of some factors considered responsible for the production of cerebral injury following prolonged insulin hypoglycemia.

The mechanism for the cerebral damage was not found to be causally related to changes in oxygen saturation of arterial blood or to the presence of marked circulatory impairment.

It was found that relatively small doses of insulin, i. e., 3 units per kilogram, resulted in prolonged hypoglycemia but did not produce cerebral injury. However, larger doses, i. e., from 15 to 20 units per kilogram, did result in widespread cerebral damage, although the hypoglycemia produced was neither more prolonged nor more severe as judged by the concentrations of the blood sugar. These results were interpreted as suggesting that the injurious effects of large doses of insulin are brought about by the promotion of some reaction in the cerebral cells which is relatively harmless if the blood sugar is maintained.

Animals under anesthesia induced by pentobarbital sodium were found to be more susceptible to the toxic action of insulin.

RECOVERY OF SYMPATHETIC NERVE FUNCTION IN SKIN TRANSPLANTS

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The restoration of sympathetic function to the skin and other tissues peripherally denervated has not been studied extensively. The increasing use of sympathectomy makes important a more precise knowledge concerning sympathetic nerve regeneration in man after various types of denervation.

Forty years ago Tuckett [1] and, later, Kilvington and Osborne [2] found evidence of regeneration after section of postganglionic fibers. Boeke and Heringa [3] observed sympathetic fibers along the ducts of the sweat glands and in close relation to the gland cells nine months after peripheral nerve section in man. Clark, Clark and Williams [4] noted regeneration of sympathetic fibers and restoration of contractility to arterioles in the rabbit's ear, as viewed through their transparent chamber. Goecke and Beaufays [5] showed an early growth of sympathetic fibers into transplanted ovaries in mice. Ford and Woodhall [6] cited the syndrome of crocodile tears and the auriculotemporal syndrome as evidence of misdirection of regenerating autonomic fibers.

From the Department of Surgery, the University of Chicago.

1. Tuckett, I. L.: On the Structure and Degeneration of Non-Medullated Nerve Fibres, J. Physiol. **19**:267, 1896.

2. Kilvington, B., and Osborne, W. A.: The Regeneration of Postganglionic Vasoconstrictor Nerves, J. Physiol. **35**:460, 1907.

3. Boeke, J., and Heringa: Nerve End Bodies and Skin Sensation in a Case of Nerve Regeneration, Proc. Roy. Acad. Amsterdam **33**:685, 1924.

4. Clark, E. R.; Clark, E. L., and Williams, R. G.: Microscopic Observations in the Living Rabbit of the New Growth of Nerves, Am. J. Anat. **55**:47, 1934.

5. Goecke, H., and Beaufays, J.: Ueber Degeneration und Regeneration des vegetatives Nervengewebes im transplantierten Ovarium, Arch. f. Gynäk. **160**: 571, 1936.

6. Ford, F. R., and Woodhall, B.: Phenomena Due to Misdirection of Regeneration Fibers of Cranial, Spinal and Autonomic Nerves, Arch. Surg. **36**:480 (March) 1938.

Only a few observations on recovery of sympathetic function in skin transplants are found recorded. Dubreuihl and Noel [7] found a positive sweating reaction in a Wolfe graft after fifteen months. Kredel and Evans,[8] at the University of Chicago Clinics, mentioned the late recovery of sweating in two pedicle flaps in a series of skin transplants studied for the recovery of sensation. A further study of this series and of those in other cases has revealed more evidence of sympathetic recovery and is the subject of the present report.

MATERIALS AND METHODS

A series of human skin transplants, chiefly pedicle flaps, were followed for evidence of sympathetic recovery for varying periods up to nine years. Sudomotor, vasomotor, pilomotor and sebomotor functions were studied and correlated with recovery of sensation. Other details in most of the cases are given in the report by Kredel and Evans.[8]

Sweating was most often tested by placing the patient in a heat cradle for a half-hour. Contact with clothing of regions to be studied was avoided. Gross beads of perspiration could usually be observed. The starch-iodine reaction was also employed in some cases. Inadequate vasomotor function was indicated by readings of skin temperature, dermatographia, persistence of blanching after pressure and changes in color of the skin. The presence of goose flesh after exposure to cold established pilomotor function.

It was also studied in 4 of the cases by Rothman, with the method of Coon and Rothman,[9] who found that acetylcholine and nicotine injected intradermally produce goose flesh. The optimal doses were 0.1 to 0.2 cc. of nicotine sulfate (1:100,000) and 0.1 to 0.2 cc. of acetylcholine (1:40,000). They found that acetylcholine and nicotine act through a short peripheral nervous mechanism, probably an axon reflex. The pilomotor action is unimpaired immediately after blocking or cutting the corresponding peripheral mixed nerve, but disappears after the nerve has degenerated. The occurrence of pilomotor action in grafts after the injection of nicotine or acetylcholine means that the peripheral nervous mechanism has been reestablished. Tests with acetylcholine and nicotine have recently been made in cases 1, 2 and 4 and produced goose flesh. In another case of pedicle flap in which tests were made fifteen months after operation there was no response to injections of acetylcholine and nicotine, although pain and tactile senses were partly regenerated.

REPORT OF CASES

CASE 1 (case 4 of Kredel and Evans).—W. B., aged 9, had a large pedicle flap of skin and subcutaneous fat, 13 by 5 cm., transplanted from the left thigh to the lower part of the right leg. Sweating tests made four months after the final stage gave normal results. At eleven months slight sweating was present

7. Dubreuihl, W., and Noel, P.: De la greffe cutanée par transplantation totale, Rev. de chir., Paris **43**:83, 1911.

8. Kredel, F. E., and Evans, J. P.: Recovery of Sensation in Denervated Pedicle and Free Skin Grafts, Arch. Neurol. & Psychiat. **29**:1203 (June) 1933.

9. Coon, J. M., and Rothman, S.: The Nature of the Pilomotor Response to Acetylcholine, Proc. Soc. Exper. Biol. & Med., to be published.

at the upper margin (fig. 1). At twenty-five months sweating was fairly extensive over the area of recovery of touch, but was absent in the lower portion. A similar result was obtained at thirty months. These tests were performed by the starch-iodine method. After five and a half years the flap was restudied by observation for gross drops of perspiration after baking the patient in the heat cradle. The first test was inconclusive, but two subsequent tests revealed gross drops over the upper portion. The rise in temperature of the flap at the conclusion of the sweating test was slightly greater than that of the surrounding skin, except for one point anterior to the flap. Thiersch grafts on the thigh were from 0.2 to 0.5 degree C. cooler than the adjacent skin and showed no evidence of sweating. Wolfe grafts applied to the interdigital spaces for correction of syndactyly, five and one-half years before, were moist. After six and a half years the lower portion of the pedicle flap on the leg was dry. There was no evidence of sebaceous secretion, and a definite pilomotor response could not be

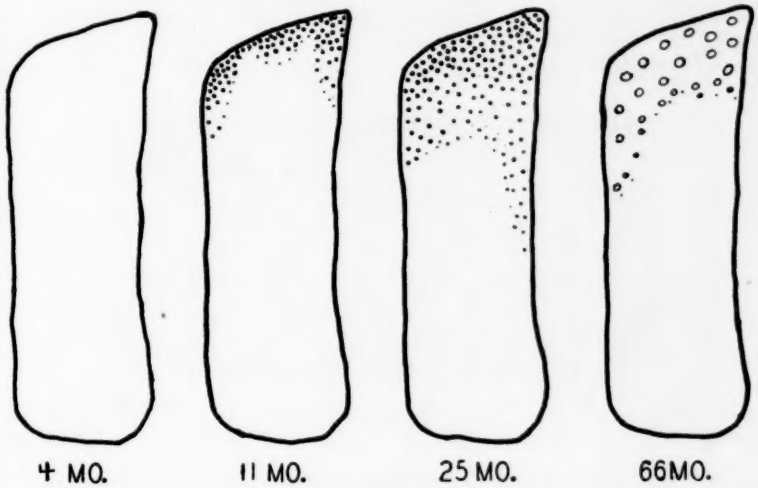

Fig. 1 (case 1).—Result of the sweating test on the skin flap. The starch-iodine test was used at four, eleven and twenty-five months. Gross drops of perspiration appeared at sixty-six months (five and a half years).

elicited, although a suggestion of goose flesh on exposure to cold was seen in the upper portion.

In this case recovery of sweating was delayed and occurred only in the upper portion of the pedicle flap. The area of recovery increased in size from eleven to twenty-five months after operation, but showed no further advance. Recovery of touch and pain sensation also remained poor in the lower portion of the flap. Wolfe grafts sweated at the end of five and a half years, while Thiersch grafts remained dry.

Recent examination eight years and two months after transplantation revealed complete return of pain and tactile senses except in a very narrow zone at the lower end. Intracutaneous injection of nicotine in scattered regions produced a marked pilomotor response (fig. 2). All of the flap except the distal margin appeared to be as oily as the normal skin.

Case 2 (case 3 of Kredel and Evans).—J. C., aged 9, had large flaps applied to the anterior and posterior aspects of the left knee for defects and contracture following extensive burns. The anterior flap, which had shown excellent return of sensation during the first year, remained free of sweating at twenty-seven and thirty-four months. A sweating test at five and a half years still failed to reveal perspiration. The posterior flap showed no obvious sweating at three years, but gave a positive response to the test at five years and ten months. Exposure of the patient for eight minutes in a refrigerator at 2 C. at this time produced definite goose flesh on the posterior flap, but none on the anterior flap. The disappearance of blanching of both flaps after pressure required approximately two seconds at three years and one second at five and a half years. The amount and duration of erythema on each flap following scratching were about the same as on the normal skin.

Postoperative examination when the posterior flap had been transplanted eight and three-fourths years and the anterior flap eight years gave the following results: In the posterior flap pain and tactile senses were restored throughout the flap, but were incomplete about the scarred periphery in some regions. Temperature sense was imperfectly restored in most of its extent. Injections of nicotine and

Fig. 2 (case 1).—Transplant eight years after operation (distal end shown at the right). Goose flesh appeared about wheals *a* and *c* one to one and one-fourth minutes after injection of nicotine. Wheal *b* is shown five minutes after injection; goose flesh appeared about it, but had disappeared in about two minutes.

acetylcholine produced goose flesh in all portions except irregularly in narrow margins. In the anterior flap pain and tactile senses were restored except irregularly about the margins of the lower half. Temperature sense was very feeble in a part of its extent and absent in the rest. Injections of nicotine and acetylcholine produced goose flesh over the entire flap, but it was somewhat less marked in the proximal than in the distal half.

The anterior flap, which was surrounded by a considerable amount of scar tissue, showed no recovery of perspiration or pilomotor function. The posterior flap recovered both functions to some extent. Thiersch grafts did not sweat after five and a half years.

Case 3.—B. C., aged 7, had a long flap with attached proximal pedicle transplanted from the back to the axilla and a second flap from the abdomen to the arm above the elbow. Sensation was restored almost to normal within one and a half years. At four and a half years a sweating test showed a slight response on the axillary pedicle, while the arm flap was moist but showed no beads of perspiration. At five and a half years the flaps showed a pilomotor response after faradic stimu-

lation and after application of ice to the back. The latter produced definite goose flesh. Both sudomotor and pilomotor functions recovered in this case.

CASE 4 (case 17 of Kredel and Evans).—C. L., aged 17, had a long tubed flap elevated on the back. The lower portion was transplanted to the under surface of the chin. The unutilized upper portion of the tube was allowed to hang free for two years, as other plastic procedures were performed.

The chin flap showed an early return of sensation. At four months some pain and touch sensation were present. At ten months both pain and touch

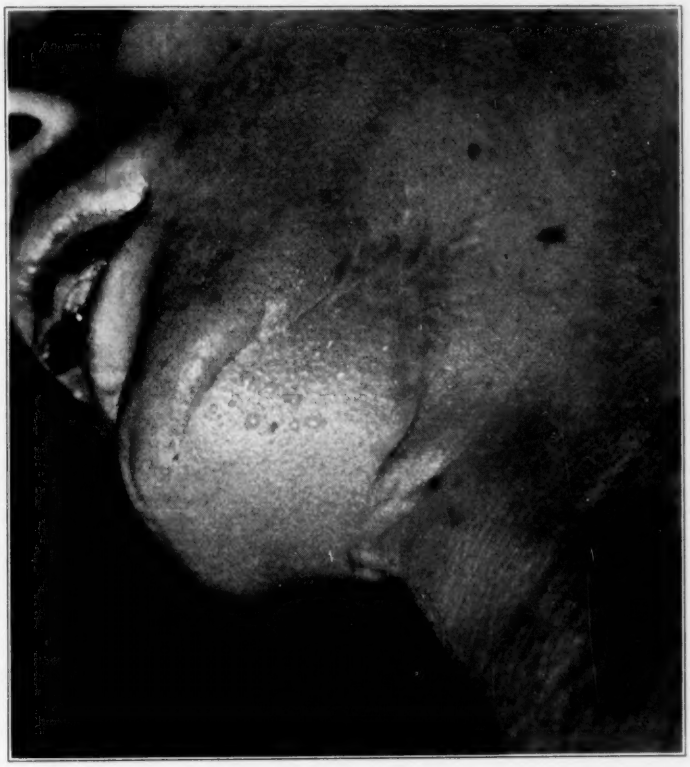

Fig. 3 (case 4).—Droplets of perspiration on a flap beneath the chin at the end of four years.

were well restored, although they were less than normal in the center, and some temperature sense was noted at the lateral borders. The flap was not moist, and the patient stated that it had not sweated even when profuse perspiration occurred on the surrounding parts of the face and neck. At ten months the temperatures of the skin of the peripheral portions were about the same as those of the surrounding skin, while the center was over 1 C. cooler. After four years a test produced profuse sweating on the chin flap, which was somewhat greater than that of the surrounding skin, but about the same as that on the back near the original donor site. Numerous large droplets were present (fig. 3). The scar at the donor site showed no moisture. The flap was still somewhat paler than the

adjacent skin. It did not blanch noticeably on pressure and showed no dermatographia. The patient expressed the belief that goose flesh had been present in winter. She stated further that exposure to cold made the flap feel heavy and abnormally cold when touched with the fingers. Sebomotor function seemed also to have returned, since the flap was as oily as the surrounding skin. This flap showed evidence, therefore, of return of all sympathetic functions in the skin. The symptoms on exposure to cold may be explained as an exaggerated vasoconstrictor response.

The tubed pedicle on the back at five months showed good appreciation of pinprick for 2 cm. at the base, with occasional responses up to 6 cm. Touch was present from 0.5 to 1 cm. Repeated tests until removal of the tube at the end of two years showed that the area of pain advanced to 8 cm. and that of touch to 2 or 2.5 cm. along the pedicle. Sweating was not tested early, but at twenty-one and twenty-four months it was noted for 3 and 2 cm., respectively. Persistent erythemic spots appeared after pinprick in the area of incomplete sensory return. They did not appear near the proximal end, where touch and sweating were present, or distal to the area of recovery of pain. The skin temperature at twenty-one months was 32.7 C. at the base of the pedicle, with a gradual rise to 34.3 C. at the free tip. The temperature of the surrounding skin was from 34.3 to 34.7 C.

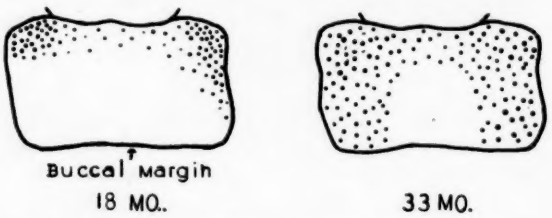

Fig. 4 (case 5).—Transplant of a visor flap to the upper lip. A test with starch and iodine was made at eighteen months. Spontaneous sweating, with beads of perspiration, appeared at thirty-three months.

Recovery of sweating, as well as of touch, occurred over a limited proximal area in this instance.

Case 5 (case 1, Kredel and Evans).—G. V., had a large visor flap taken from the scalp to replace the upper lip, which was removed because of carcinoma. The internal surface was lined by a Thiersch graft, so that the flap was attached only at its superior and lateral margins. At six months compression of the flap by rotating it upward produced blanching, which after release was gradually replaced by flushing. Injection of epinephrine into the flap caused localized blanching, while pilocarpine, atropine and histamine had no effect. A sweating test at eighteen months showed a good response at the upper right corner and along the left lateral margin. Rare spots of moisture were present over the upper half. The lower third remained entirely dry in the starch-iodine test. The amount of sweating in the recovered area was not as marked as on the normal skin. At thirty-three months, on a warm day, spontaneous sweating, with beads of perspiration, was noted over the lateral and superior portions of the flap. The center and the medioinferior portion, down to the free buccal margin, did not sweat (fig. 4). The flap was not significantly paler than the surrounding skin. Blanching after digital pressure recovered within one to two seconds.

In this case recovery of sweating at thirty-three months had advanced about 3 cm. from the attached margins. Sensation had returned practically to normal after eighteen months, although recovery had been somewhat delayed in the central and inferior portions.

CASE 6 (case 11 of Kredel and Evans).—M. N., aged 17, had a large flap transplanted from the abdomen to the dorsum of the left hand, with recovery of sensation to pinprick, cotton wool and differences in temperature in two months. After four years observation on a hot afternoon revealed definite sweating on the flap. The patient had previously noted beads of perspiration, particularly in the center. Release of a constrictor applied to the arm for two minutes resulted in moderate, but not excessive, reactive hyperemia on the flap. Dermatographia was rather marked. Pricking and scratching with a pin produced wheals in ten minutes. The patient reported that exposure to cold in winter caused the graft to become blue. In this case good recovery of sudomotor activity was shown, while vasomotor function remained impaired.

CASE 7 (case 6 of Kredel and Evans).—In the case of H. K., aged 14, a flap was transplanted from the thigh to the left heel posteriorly, running transversely. Observations at four, eight, ten and twelve months showed no evidence of moisture. At twenty-six months the flap was definitely moist, and the patient had observed sweating. At twenty-eight months erythemic spots appeared after pinprick on the lower portion of the flap. This region had shown poor recovery of sensation, especially for touch, and there had developed at one period a superficial ulcer from pressure of the shoe. At four years the flap was noted to be warm, moist and of good color. At six years vasomotor function had incompletely recovered. A persistent red flush occurred after hot baths. Blanching on pressure disappeared immediately over the upper half, as on the normal skin, but persisted for two to three seconds in the lower portion. Dermatographia after scratch remained for fifteen minutes. In this case sweating was recovered to some extent within twenty-six months, but vasomotor return remained incomplete after six years. The impairment was most marked over the area with poor recovery of sensation to light touch.

CASE 8.—E. B., aged 43, had a pedicle flap transplanted from the abdomen to the dorsal surface of the left forearm. At eight and one-half months the flap showed no evidence of sweating. Blanching on pressure persisted for ten to fifteen seconds. Some return of sensation for pain had occurred, but none for touch or temperature. At twenty-two months there was no recovery of touch. The area of recovery of pain was limited to the radial third. On palpation a sweating test produced neither droplets nor moisture on the flap. The temperature of the flap after the test rose no higher than that of the normal skin to the side and distally. However, marked erythema occurred. This gradually faded, with the appearance of blotchy, pale areas progressing from the ulnar to the radial side.

In this case no recovery of sweating occurred in twenty-two months. Vasomotor function remained abnormal.

CASE 9 (case 2 of Kredel and Evans).—In the case of T. S., a visor flap replaced the lower lip, which was removed for carcinoma. Early recovery of both pain and touch sensation took place. During ten months' observation sweating was not seen, although tests were not performed. At six months the flap was

noted to be less pale than formerly, and blanching on pressure disappeared quickly. Some recovery of vasomotor function was present. At twenty-six months a radium pack was applied to the upper border for a local recurrence of carcinoma. No injury to the flap resulted from exposure of 500 mg. hr.

CASE 10 (case 10 of Kredel and Evans).—In the case of L. G. a large gauntlet flap was transplanted from the abdomen to the dorsum of the hand. At three and a half years, blanching of the skin quickly disappeared after release of pressure. Vasomotor tone was good.

CASE 11 (case 9 of Kredel and Evans).—W. S. had had an oblique flap transposed from the thigh to the medial side of the ankle eleven years previously. Recovery of sensation to pinprick was absent in the posteroinferior quarter of the flap, but was present elsewhere. There was no recovery of touch or temperature sense. Persistent local areas of erythema appeared about the points pricked by a pin. Vasomotor function was abnormal. Permission for a sweating test was refused. The patient stated he had not observed perspiration on the flap.

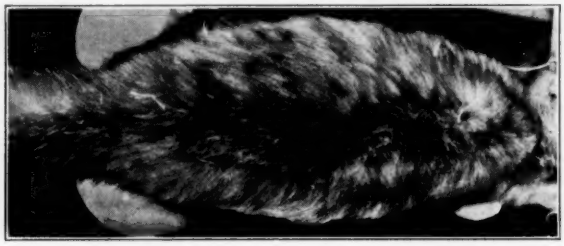

Fig. 5.—Recovery of erection of hair on the dorsum of a cat after two and a half years. The hypothalamus was stimulated electrically. The four corners of the flap are marked by white string tied to the hair.

PILOMOTOR RESPONSE IN ANIMALS

In each of 2 young cats a large flap was elevated in stages on the left side of the back and resutured in the same position. An area of skin and subcutaneous tissue, 20 by 5 cm., was thus completely denervated. Monthly determinations of pilomotor response by the fright test showed no erection of hair on the flap during the first seven months. Slight erection of hair occurred at eight months. At ten and fourteen months the responses seemed about the same on the flap as on the normal side. However, since the cats had become rather unresponsive, the tests were not completely satisfactory. Response to pinprick was present at fourteen months and the skin temperature of the flap averaged only 0.1 degree C. higher than that on the opposite side. After two and a half years Dr. N. Keith Bradford performed direct stimulation of the hypothalamus with the Horsley-Clarke stereotaximeter. Marked erection of hair on the flap in each case was about as extensive as on the normal side (fig. 5). Histologic sections prepared by the Gros method demonstrated reinnervation of both the blood vessels and the arrectores pilorum muscles. Regeneration of sympathetic fibers in skin flaps was also demonstrated in the rabbit.

COMMENT

These cases demonstrate that a considerable amount of sympathetic nerve function may return to transplanted pedicle skin flaps. Variability in the rate and extent of recovery is marked. Adequate return of associated sensation, particularly of light touch, seems a necessary factor in sympathetic recovery. In case 1, in which there was considerable delay in return of light touch distally, sweating was not recovered in the lower portion. In case 8, in which there was no recovery of touch, there was no sweating at twenty-two months. In case 7 delayed and incomplete recovery of touch and of sympathetic functions was shown in the lower portion of the flaps. In the tubed pedicle in case 4 sweating was recovered only over the basal area of recovery of touch. The presence of deep scarring about a flap limits sympathetic as well as somatic nerve regeneration to all or to parts of a flap.

Return of sudomotor and sebomotor function may be of some practical importance in keeping a flap clean. If the skin is completely dry, particles of dirt become caked in the folds of the skin as well as in the hair follicles and are difficult to remove except by vigorous scrubbing. The patients in cases 1, 4 and 7 had some annoyance in this regard. However, infection was not observed to result from accumulation of dirt. On exposed portions of the body, particularly on the face, inadequate vasomotor function results in variations in color of the skin, which are undesirable from a cosmetic standpoint. Some of these vasomotor disturbances may persist if abnormal regeneration of sympathetic nerves to blood vessels has occurred. Ford and Woodhall [6] mentioned autonomic dysfunction after injury to peripheral nerves. One of us (F. E. K.) has the auriculotemporal syndrome, which followed dislocation of the temporomandibular joint twenty-five years ago. Flushing and excessive sweating over the parotid region after eating have persisted. Some of the flaps in this series have remained hypersensitive to cold.

The failure of thin free grafts to recover skin secretions is explained by the fact that much of the sweat and sebaceous glands is left behind, as well as by inadequate nerve regeneration due to fibrosis of the bed. Apparently, the small amount of duct epithelium included in thin grafts prevents regeneration of functional secreting glands in Thiersch grafts. To what extent sweating may be recovered in the thicker types of free grafts deserves further study.

We have observed some return of sweating several years after lumbar and cervicothoracic sympathectomy for Raynaud's disease.

CONCLUSIONS

1. Recovery of sympathetic function is a late manifestation of nerve regeneration in pedicle skin flaps. The earliest return of sweating was at eleven months.

2. The extent and rate of recovery are variable. In some cases there is no evidence of sudomotor activity after many years.

3. Early and adequate recovery of cutaneous sensation is usually, but not invariably, followed by recovery of sympathetic function. When only a portion of a flap recovers sweating the area often corresponds to that for the recovery of light touch. This indicates that sensory and sympathetic fibers grow out along the same pathways.

4. Vasomotor function usually returns to some extent but, like sweatting, often remains impaired. Dermatographia, persistence of blanching after pressure, prolonged erythema after exposure to heat and hypersensitiveness to cold are common signs of inadequate vasomotor function in skin transplants.

5. Pilomotor and sebomotor functions may recover.

6. Free transplants show little evidence of return of sympathetic function. Thiersch grafts have shown no return. In 1 case Wolfe grafts sweated slightly.

7. Pilomotor function recovers in the peripherally denervated skin of the cat. There is anatomic evidence of regeneration of sympathetic fibers to the blood vessels and the errectores pilorum muscles in the skin.

SUMMARY

Recovery of sympathetic function is described in a series of pedicle skin flaps in man. Sudomotor, vasomotor, pilomotor and sebomotor functions may recover. The amount of restoration parallels to some extent the recovery of cutaneous sensation. Return of pilomotor function and regeneration of sympathetic fibers occur in the peripherally denervated skin of the cat.

PALATAL MYOCLONUS

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Palatal myoclonus is a relatively rare and still obscure phenomenon, and therefore it is necessary to collect all cases one observes, especially if the condition has been verified by postmortem examination. We have had the opportunity of observing 4 cases of palatal myoclonus and of making an anatomic examination in 1 of them.

Leshin and Stone;[1] Hillemand, Chavany and Trelles;[2] Davison, Riley and Brock,[3] and Guillain and Mollaret[4] have given excellent surveys of the literature. Therefore we shall not mention all the recorded cases. Since 1935, the following have reported cases with an anatomic study: Alajouanine, Thurel and Hornet;[5] Marinesco, Jonesco-Sisesti and Hornet;[6] de Savitsch;[7] Lhermitte and Drouzon;[8] de Savitsch and Ley,[9] and Nicolesco, Sager and Hornet.[10]

However, we must mention some older publications which have not met with the attention they deserve. First, as early as 1902, Klien[11] described continuous rhythmic contractions of the palate, pharynx, larynx, tongue and diaphragm; in 1 case there were also contractions of

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1. Leshin, N., and Stone, T. T.: Continuous Rhythmic Movements of the Palate, Pharynx and Larynx, Arch. Neurol. & Psychiat. **26**:1236 (Dec.) 1931.
2. Hillemand, P.; Chavany, J. A., and Trelles, O.: Rev. neurol. **64**:1, 1935.
3. Davison, C.; Riley, H. A., and Brock, S.: Bull. Neurol. Inst. New York **5**:94, 1936.
4. Guillain, G., and Mollaret, P.: Études neurologiques: Les myoclonies vélo-pharyngo-laryngo-oculo-diaphragmatiques—La maladie de Friedreich—Pathologie du névraxe, Paris, Masson & Cie, 1936.
5. Alajouanine, T.; Thurel, R., and Hornet, T.: Rev. neurol. **64**:853, 1935.
6. Marinesco, G.; Jonesco-Sisesti, N., and Hornet, T.: Rev. neurol. **66**:541, 1936.
7. de Savitsch, E.: J. belge de neurol. et de psychiat. **36**:291, 1936.
8. Lhermitte, J., and Drouzon, J.: Rev. neurol. **67**:390, 1937.
9. de Savitsch, E., and Ley, R. A.: Rev. neurol. **67**:585, 1937.
10. Nicolesco, J.; Sager, O., and Hornet, T.: Rev. neurol. **70**:301, 1938.
11. Klien, H.: Deutsche med. Wchnschr. **28**:665, 1902; Neurol Centralbl. **26**: 245, 1907; Monatschr. f. Psychiat. u. Neurol. **43**:79, 1918; **45**:1, 1919.

the intercostal muscles. In 3 cases Klien made a minute anatomic examination and observed lesions in the white matter of the cerebellum with involvement of the dentate nucleus. Klien described also the degeneration of the olive with "swelling" (pseudohypertrophy), contralateral to the cerebellar lesion. He insisted that in his cases the central tegmental tract was undamaged. (We wish to emphasize that the central tegmental tract was first described by Bechterew in the laboratory of Flechsig in Leipzig, in 1883, where Klien, also, made the anatomic study in his cases.)

Moreover, in their case, Oppenheim and Siemerling [12] described "small, continuous, nearly rhythmic contractions of the palate." At postmortem examination they observed an aneurysmal dilatation of the left vertebral artery, with softening of the adjacent medulla through compression by the aneurysm. The softening involved the left pyramis and the left olivary nucleus.

As to the cause of palatal myoclonus, in the majority of cases there was a vascular process at the base—hemorrhage or softening. In 5 cases only, e. g., those of Spencer,[13] Oppenheim,[14] Freeman,[15] de Savitsch and Ley [9] and Schmitt,[16] were there tumors of the cerebellum or the pontocerebellar angle. In 1 case there was multiple sclerosis (Leshin and Stone [1]); in 1, epidemic encephalitis (Lévy,[17]); in 1, encephalomyelitis (Guillain and Mollaret [4]), and in 1, trauma (Pfeifer [18]).

The anatomic problem or the problem of localization has been studied most. There are two groups of cases: In one the lesions are in the tegmentum of the pons, where the central tegmental tract especially is damaged and degenerated, and in the other, in the cerebellum, involving the dentate nucleus.

The physiopathologic problem of palatal myoclonus is still obscure. Perhaps the mechanism is a release of physiologic inhibition exercised under normal conditions on the bulbar nuclei by a higher center. It is noteworthy that myoclonic movements in the syndrome under discussion involve the muscles concerned with respiration and swallowing. Freeman [15] expressed the idea that the myoclonic movements of these muscles have the closest approximation to the act of yawning; he called this form of myoclonus "miniature yawning."

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12. Oppenheim, H., and Siemerling, E.: Charité-Ann. **12**:331, 1887.
13. Spencer, H. R.: Lancet **2**:702, 1886.
14. Oppenheim, H.: Neurol. Centralbl. **8**:132, 1889.
15. Freeman, W.: Palatal Myoclonus: Report of Two Cases with Necropsy, Arch. Neurol. & Psychiat. **29**:742 (April) 1933.
16. Schmitt, W.: Nervenarzt **5**:456, 1932.
17. Lévy, G.: Contribution à l'étude des manifestations tardives de l'encéphalite épidémique (formes prolongées et reprises tardives): Syndrome excitomoteur—syndrome parkinsonien, forme respiratoire, forme insomnique et hypomaniaque de l'enfant, Thesis, Paris, no. 439, 1922.
18. Pfeifer, R. A.: Monatschr. f. Psychiat. u. Neurol. **45**:96, 1919.

ANATOMIC REPORT OF A CASE

CASE 1.—J. N., a man aged 77, was examined by us in the Hospital of the Brothers of St. John of God, on Sept. 26, 1936. Unfortunately, the patient was in such a state of apathy and his speech was so unintelligible that we could not learn the history of his illness. Moreover, he had no relatives and nobody came to see him, so that we did not secure any information about his disease. The patient was so uncooperative, too, that it was impossible to make as complete an examination as would have been desirable, and we regret that our report is incomplete.

Physical Examination.—The right pupil was irregular and wider than the left, but both pupils reacted to light. There was hemiplegia on the right side, including the face. The right limbs were hypertonic. The right leg had been shorter than the left since childhood. The patient was bedridden; he could neither stand nor walk. The tendon reflexes were increased on the right side and normal on the left. The abdominal reflexes were present and equal on the two sides. There was a positive Babinski sign on the right. Speech was indistinct and nearly unintelligible.

The most interesting phenomena were continuous rhythmic twitchings of the soft palate and pharynx. On inspecting the oral cavity, one saw rhythmic twitchings of the soft palate, the uvula being drawn to the right and upward. The posterior pharyngeal wall was drawn synchronously to the right. These myoclonic movements were strictly unilateral and on the right side. The rate of the twitchings was about 128 per minute. We did not see rhythmic movements of the eyes, face, tongue or intercostal muscles; it was impossible to examine the larynx and the diaphragm.

The arterial pressure was 170 systolic and 80 diastolic. The Wassermann and other serologic reactions of the blood were negative.

Diagnosis.—The patient showed the clinical picture of pseudobulbar paralysis, with hemiplegia and myoclonic movements of the palate and pharynx on the right side.

The patient died on Oct. 12, 1936.

Macroscopic Examination.—Frontal Sections of the Brain: A section passing through the optic thalamus behind the gray commissure revealed at the superior pole of the external nucleus of the thalamus a cavity measuring 5 by 2 mm., involving on its superior pole the caudate nucleus and on its lateral side the capsula interna. In the vicinity of the cavity the internal capsule was spongy. There were several small postmalacic cysts in the middle and posterior part of the putamen and pallidum on both sides.

The cerebellum was cut into sections strictly vertical to the longitudinal axis of the pons and medulla. In a section (fig. 1) passing through the posterior end of the sulcus interlobaris and the medulla in the middle part of the olives, there was an area of old hemorrhage in the white matter of the right hemisphere, which occupied nearly the whole center of the white substance. The ventral and lateral parts of the dentate nucleus were destroyed by this lesion.

The macroscopic appearance of the pons was normal. The left olive of the medulla showed hypertrophy. The spinal cord was normal.

Microscopic Examination.—Spinal Cord: In the spinal cord there was no degeneration of Helweg's olivospinal tract, the spinocerebellar tracts or the pyramidal tracts. Staining with scarlet red revealed nothing abnormal.

Medulla Oblongata (fig. 2): On the left there was pseudohypertrophic degeneration of the olive, both in the ventral and in the dorsal lamina; changes in the mesial accessory nucleus were less marked; the dorsal accessory nucleus was undamaged. The periolivary fibers, especially the fibers of the hilus, were

diminished. There was slight degeneration of the central tegmental tract. The pyramidal tract was normal.

Scarcely one of the ganglion cells of the left olivary nucleus was normal. One could follow several stages of the cellular alterations (fig. 3), from simple swelling

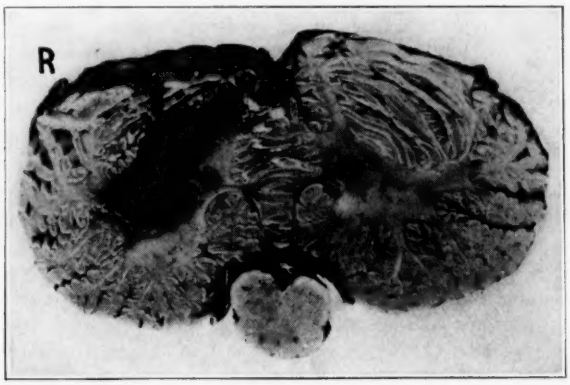

Fig. 1.—Section through the inferior part of the cerebellum and medulla, showing hemorrhage in the right hemisphere.

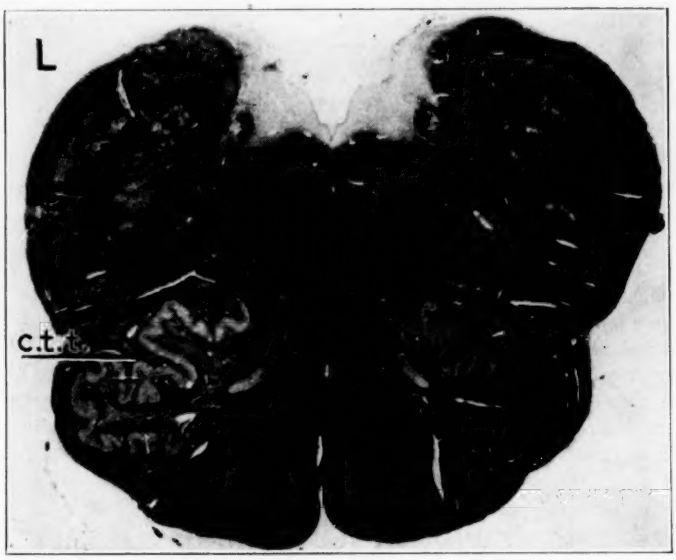

Fig. 2.—Section through the middle of the medulla, showing hypertrophy of the left olive. Here, *c. t. t.* indicates the central tegmental tract.

of the cell body to formation of so-called windows (*fenêtres* of French authors), which enabled us to make a dynamic reconstruction of the pathologic process. The part of the cell in which the lipochrome lies swelled first. The volume of the cell increased; the nucleus became eccentric. The Nissl substance about the nucleus

stained well for a long time, but showed tigrorhexis and later tigrolysis, which extended from the periphery to the center of the cell body. In the cells of a larger type the Nissl substance formed large grains, which stained well and were more resistant to the progressive degenerative process. In the first stage of hypertrophy the dendrites became more visible than in the normal state. The Bielschowsky method gave the best and most instructive results; it showed most clearly the

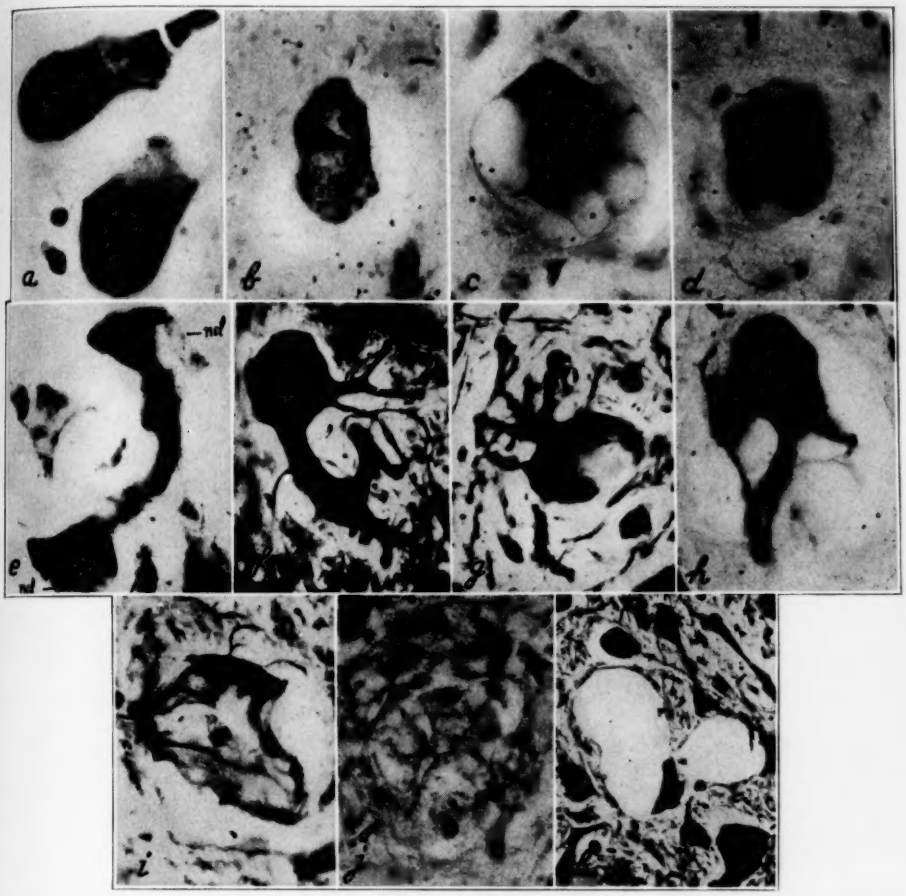

Fig. 3.—Alterations of the cells of the olivary nucleus, according to their propressive development. Sections *a, d* and *h* were prepared by the Nissl method; *e, f, g, i* and *k*, by the Bielschowsky method, and *j*, by the hematoxylin and Van Gieson stain. In *d* and *e* binuclear nerve cells are shown. In *e, ncl* indicates the nucleus.

state of the dendrites. They were swollen and contracted in a nearly ameboid manner; they surrounded the cell body and gave the impression of a basket or glomerulus. In the second stage, it was in the lipochrome again that the formation of vacuoles took place. In the beginning the vacuoles were numerous and small;

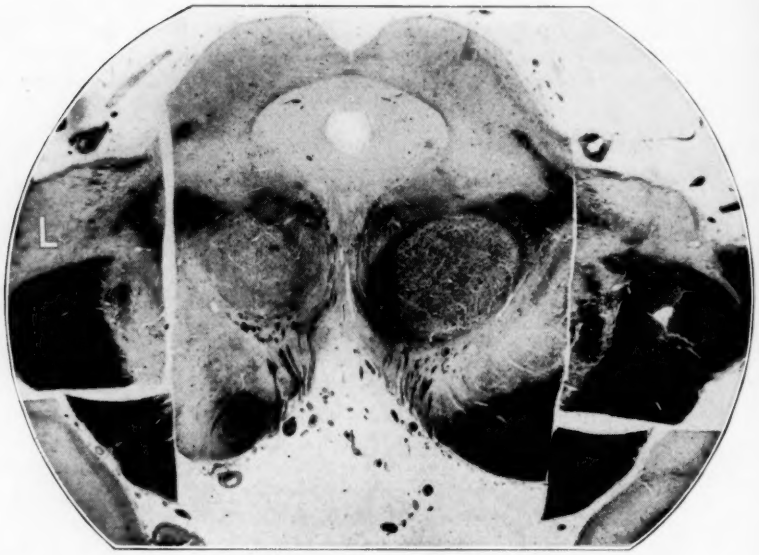

Fig. 4.—Section through the peduncles and the red nuclei, showing atrophy of the left red nucleus.

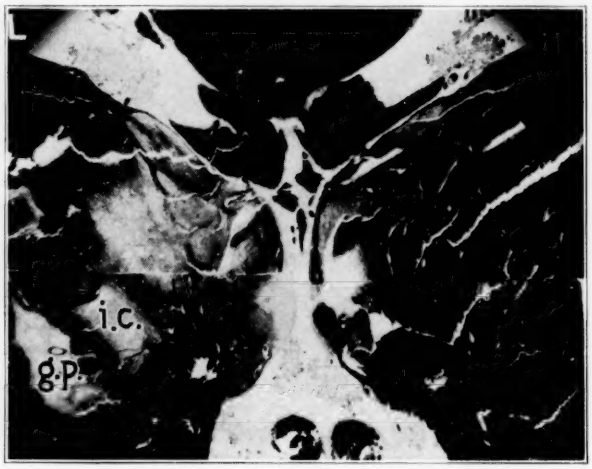

Fig. 5.—Section through the diencephalon, showing lesions in the thalamus opticus, internal capsule (*i. c.*) and globus pallidus (*g. p.*).

then their volume increased progressively and they coalesced, so that at the end of this stage the cell, being of gigantic dimensions, was represented only by vast vacuoles with very thin membranes and the clear, but well stained, nucleus and its nucleolus. The lipochrome had vanished, and of the Nissl substance there was only a remnant about the nucleus, the latter being usually displaced to the periphery of the cell and surrounded by the vacuoles on two or several sides. It is to be observed that from their first appearance the vacuoles were destitute of all morphologic content, as well as of all stainable colloidal or argentophilic substance. The cells of a smaller type were sometimes represented by a single large vacuole, the nucleus forming a crescent. The final picture of the cellular pseudohypertrophy was represented by bursting of the vacuoles, vanishing of the cell body and formation of the "window"—a unilocular or multilocular cavity in the nerve tissue. For some time one could see in the "window" membranous remnants of the body and of the nucleus. The most resistant part was always the nucleolus. Besides the vacuolar degeneration of the nerve cells, one could see cells undergoing simple atrophy, even *Zellschatten.*

Fig. 6.—Section through the cerebellum. Lesion in the white matter of the right hemisphere, involving the dentate nucleus.

The reaction of the microglia and oligodendroglia was poor. There was no real neuronophagia. The macroglia cells showed an increase in number and volume, especially the protoplasmic astrocytes. The reaction of the fibrous glia was well marked. The protoplasmic astrocytes sometimes enveloped the vacuolated cells or "windows" with their dendrites.

There were no vascular alterations in the region of the olives.

The right olivary nucleus was normal. Only in some nerve cells of the mesial accessory nucleus did one observe swelling of the cell body, with destruction of the Nissl substance in the periphery. Marked degeneration was seen in the restiform body. The pyramidal tract was normal.

Pons: The tegmentum was free from all focal lesions. In the region of the central tegmental tract the slight degeneration observed in the medulla was not to be seen; staining with scarlet red also gave negative results. There was degeneration of the right superior cerebellar peduncle. The medial longitudinal bundle, the lemniscus and the pyramidal tracts were normal.

Cerebral Peduncles: Inferior part: The fibers of the decussation of Wernekinck were reduced on the left side. There were no focal lesions. In sections

of this region, on the left side of the basis, one observed for the first time degeneration affecting the lateral part of the frontopontile pathways and the adjacent part of the medial corticobulbar pathways.

Middle and superior parts (fig. 4): In all sections passing through the red nucleus one observed that the center of the nucleus on the left side was much reduced and demyelinated. The perirubral fibers had nearly vanished, especially on the ventrolateral and ventromedial sides. There was no focal lesion.

Diencephalon, left side: From the proximal pole of the red nucleus one could trace an area of demyelination in the internal nucleus of the optic thalamus, extending in a proximomedial direction to the ventricular surface of the thalamus above the taenia thalami. In a higher section (fig. 5) nearly the whole optic thalamus was demyelinated. In this section there was also a lesion in the globus pallidus. There was degeneration of the pyramidal tracts in the inferior half of the capsula interna. On the right side there were no lesions and no degenerations.

Cerebellum (fig. 6): Right side: The large necrotic area already described macroscopically destroyed completely the middle third of the white matter of the hemisphere in its entire proximodistal extent. The ventrolateral part of the dentate nucleus was destroyed by the lesion. The periciliary and extraciliary fibers had completely vanished. The nerve cells were relatively well preserved; they were partly in a state of slight swelling and partly in a state of simple atrophy. There was no vacuolar degeneration. There was cicatricial retraction of the ependyma of the fourth ventricle, where the lesion reached the ventricular surface. Everywhere there was pronounced glial reaction. The scavenger cells were loaded with products of disintegration.

Left side: The dentate nucleus was normal. In the dorsomedial angle of the white matter there was a small area, which was only slight and recent, in which the myelinated fibers cleared up.

COMMENT

In our case anatomic study revealed a lesion in the right cerebellar hemisphere, the dentate nucleus and the adjacent white matter; pseudohypertrophy of the left olivary body; degeneration of the right restiform body and the right superior cerebellar peduncle, and atrophy of the left red nucleus.

The same anatomic syndrome has been found by van Bogaert and Bertrand [19] in their case and by Klien [11] in 3 cases. Moreover, there exists a purely anatomic observation recorded by Schaffer,[20] without any clinical history of the case. Therefore, it seems to us that we are dealing here with a typical anatomic syndrome: The primary lesion was in the cerebellum, at the level of the dentate nucleus, secondary alterations being degeneration of the superior cerebellar peduncle, atrophy of the red nucleus contralateral to the side of the damaged dentate nucleus, pseudohypertrophy of the contralateral olive (contralateral also to the damaged dentate nucleus) and degeneration of the restiform body.

Three localizations of focal lesions have been considered as the cause of palatal myoclonus: the olivary nucleus, lesions in which have been seen in almost every case of palatal myoclonus; the central tegmental

19. van Bogaert, L., and Bertrand, I.: Rev. neurol. **1**:203, 1928.

20. Schaffer, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **30**:70, 1915.

tract, and the cerebellum, especially the dentate nucleus. As our case belongs in the last group, we shall discuss this group first.

In cases of this type the pseudohypertrophy of the contralateral olive has been considered as secondary to the primary cerebellar lesion, or lesion of the dentate nucleus, and it has been supposed that there is a connection between the dentate nucleus and the contralateral olive, the olivodentate fibers. Certainly, there are connections between the olive and the cerebellum, and Schaffer,[20] as well as Klien,[11] expressed the belief that there are olivocerebellar and cerebello-olivary fibers. The majority of authors have asserted that the olivocerebellar fibers end in the cerebellar cortex. André-Thomas [21] wrote that the termination of the olivary fibers has not yet been definitely established, and several authors have insisted on the existence of olivocortical fibers.

In all the cases of cerebellar lesions with palatal myoclonus previously mentioned, not only the dentate nucleus but also a more or less extensive part of the white matter of the cerebellar hemisphere adjacent to the dentate nucleus was damaged. Perhaps, therefore, it is not the lesion of the dentate nucleus that is the cause of the myoclonic movements and of the olivary pseudohypertrophy, but the interruption of the olivocerebellar and cerebello-olivary pathways. Klien,[11] especially, expressed this idea in his paper of 1919, in which he gave a minute anatomic description of the last of his cases. In our case, too, the cerebellar lesion involved not only the dentate nucleus but also a large part of the adjacent white matter.

As to the central tegmental fasciculus, we emphasize that it was slightly degenerated in our case, but the degeneration was so slight that we do not think it could be answerable for the clinical symptom of palatal myoclonus. We might consider this degeneration of the central tegmental tract as secondary to the involvement of the olivary body or—what seems more likely—to the previously described lesions of the optic thalamus and caudate nucleus. For the central tegmental tract contains not only fibers connecting the red nucleus and the olive but also fibers passing from the optic thalamus, perhaps also from the corpus striatum, to the olive.

As we have mentioned, in many cases of palatal myoclonus a lesion of the central tegmental tract, with pseudohypertrophy of the olive, has been observed, and it has been supposed that this lesion was the basis of the clinical symptom. This was the idea expressed especially by Foix. But there are cases in which this lesion was not associated with palatal myoclonus. We have found 3 instances of this kind in the literature: 1 case of Lhermitte, Haguenau and Trelles; [22] 1 of Trelles, Suarez and

21. André-Thomas: Cervellet, in Roger, G. E. H.; Widal, F., and Teissier, P. J.: Nouveau traité de médecine, Paris, Masson & Cie, 1925, pt. 19.

22. Lhermitte, J.; Haguenau, J., and Trelles, J. O.: Rev. neurol. **63**:229, 1935.

Mendez,[23] and 1 of Trelles, Mendez and Jimenez.[24] In these cases the central tegmental tract was totally destroyed and the olive hypertrophied, in the first case by softening and in the other 2 by a tuberculoma. No palatal myoclonus was present, however, in these cases. Still another negative case, that of Alajouanine, Hornet and Thurel, has, so far as we know, been reported only by title ("Tubercule protubérantiel avec lésion du faisceau central de la calotte; intégrité des cellules olivaires. Absence du syndrome myoclonique").[25] Lhermitte, Haguenau and Trelles [22] gave an explanation for their case; they expressed the belief that complete destruction of the central tegmental tract prevents production of myoclonic movements; in other terms, a minimum of fibers of this tract must be spared in order that palatal myoclonus may make its appearance.

Finally, the olivary lesion has been considered to be the cause of palatal myoclonus. The purest case of a primary lesion of the olive, in our opinion, is that of Oppenheim and Siemerling.[12] Lhermitte and Trelles [26] expressed the opinion that the lesion must show true hypertrophy of the olivary cells in order that myoclonus may appear. However, in the case of Oppenheim and Siemerling just cited there was no hypertrophy of the olive.

Guillain and Mollaret [4] drew a triangular figure showing the nuclei and pathways concerned with myoclonus. This triangle is formed by the red nucleus, the olivary nucleus and the contralateral dentate nucleus; the interconnections are the central tegmental tract, the superior cerebellar peduncle and the olivodentate fibers. Recently, they expressed the opinion that only the inferior side of this triangle, the olivodentate system, is important for the appearance of myoclonus.

The microscopic alterations of the nerve cells in the olivary nucleus seen in our case correspond with those described by other authors. We might account for their polymorphism by assuming that the various changes were merely stages of the same anatomic process. We agree with Alajouanine, Thurel and Hornet [5] that the hypertrophy and the apparent multiplication of the dendrites were not a development of new dendrites (*paraphytose* of Lhermitte). Therefore, we prefer to call these alterations pseudohypertrophy. We might, like Schaffer,[20] explain the rapid course of this process by double cellular degeneration, i. e., retrograde degeneration by interruption of the olivocerebellar pathway and, at the same time, transneuronal or transsynaptic degeneration by interruption of the cerebello-olivary fibers. Nicolesco, Sager and Hornet [10]

23. Trelles, J. O.; Suarez, L., and Mendez, M.: Rev. neuro-psiquiat. **1**:51, 1938.

24. Trelles, J. O.; Mendez, M., and Jimenez, J.: Rev. neuro-psiquiat. **1**:135, 1938.

25. Alajouanine, T.; Hornet, T., and Thurel, R.: Rev. neurol. **69**:384, 1938.

26. Lhermitte, J., and Trelles, J. O.: Encéphale **28**:588, 1933.

recently expressed the idea that the pseudohypertrophy is a special reaction of certain nerve cells to a pathologic process.

As an incidental interesting observation, we illustrate (fig. 3, *d* and *e*) two binuclear nerve cells which we observed in the hypertrophied olive, but we do not wish to draw any conclusions from this as to the pathologic process.

CLINICAL CASE REPORTS

We add personal observations, purely clinical, in 3 cases of palatal myoclonus.

CASE 2.—J. K., a man born in 1874, became ill on Jan. 5, 1930, when on awakening he felt giddy and experienced numbness in his right arm and leg. On examination the right limbs were weak; an Oppenheim sign was slightly indicated on the right side. Roentgen examination revealed dilatation of the aorta. The arterial pressure was 225 systolic and 115 diastolic. The patient had diabetes. In time his state became worse; he complained of weakness of his right limbs and clumsiness of his right fingers and could not button his clothes. Ataxia and adiadokokinesia were present in the right upper limb. There was astereognosis in the right hand.

On Jan. 19, 1936, the state of the patient was much worse. Gait and speech had continued to deteriorate. There were spasmodic laughing and weeping. There was slight central paresis of the face. The muscles of all four limbs were hypertonic. The knee jerks were increased on both sides, more on the right. An Oppenheim sign and ankle clonus were present on the right side. There was a Babinski sign on both sides, more marked on the right. The abdominal reflexes were absent on both sides. It was impossible to examine the sensibility. Speech was indistinct. The gait was shuffling; the patient walked with short steps and flexed knees, the trunk being bent double. In the left half of the posterior wall of the pharynx, rhythmic twitchings were observed, the wall of the pharynx being drawn to the left. The pulse rate was 112; the systolic pressure was 200. The patient died soon after this examination. No postmortem examination was made.

CASE 3.—K. M., a man aged 52, was admitted to the Hospital of the Brothers of St. John of God on March 21, 1938, complaining of fits of vertigo, of thirteen years' duration. In May or June 1937, on getting up one morning, he felt a sensation of weakness in his right leg; he could not stand upright and fell. There was a sensation of pins and needles in his right limbs. Speech was unintelligible. After this time his right limbs were somewhat weak; his gait was unsteady and he complained of headaches. He denied having had any venereal infection.

Neurologic Examination.—The pupils were regular and equal; they reacted to light but responded better in convergence. The ocular fundi were normal. The movements of the eyes were normal. There was slight nystagmus in the extreme lateral positions of the eyeballs. On protrusion the tongue deviated slightly to the left. The tendon and periosteal reflexes in the upper limbs were increased. There was a spastic flexor reflex of the fingers of both hands. The knee jerks were increased on both sides; the ankle jerks were present; there was a positive ankle clonus on the right, but no Babinski sign on either side. The abdominal reflexes were present. The facies was somewhat stiff, and there was loss of mimical expression. Romberg's sign was negative. The voice was slightly snuffling and indistinct. Sensibility to touch, pain, temperature and vibration was diminished over the whole right half of the body, including the face. Perception

of movements was unimpaired, and the patient recognized figures written on his skin. Stereognosis was intact in both hands. The corneal reflex was present on both sides. The masseter reflex was increased, more on the right side. The vestibular apparatus was normally excitable on both sides. Hearing was slightly diminished on the right. Smell was normal.

On inspection of the oral cavity, one observed rhythmic twitchings of the palate, with a rate of about 120 per minute. The rhythm was not absolutely regular. The myoclonic movements were strictly unilateral and on the right side. They took place in such a way that the velum was drawn up and to the right. The uvula followed passively, but was not animated by proper movements of its own. The right palatal arch was narrower and lower than the left. On phonation the palate moved normally. The pharyngeal reflex was absent. On laryngoscopic examination one saw rhythmic movements of the whole right half of the larynx, synchronous with the palatal twitchings. The laryngeal myoclonic movements were strictly unilateral, also, and on the right side. We did not find any myoclonic movements of the eyes, tongue, intercostal muscles, face or diaphragm (repeated roentgen examinations).

The arterial pressure was 230 systolic and 110 diastolic, and the pulse rate, 84. Serologic examination of the blood and cerebrospinal fluid gave negative results.

The patient is still under observation. The clinical picture has not changed essentially; there have recently been added rhythmic synchronous twitchings of the posterior wall of the pharynx on the right side.

CASE 4.—E. J., a man aged 56, who consulted us on Oct. 6, 1938, had become ill on April 26, 1935, when, during the act of defecation, the right limbs suddenly became paralyzed. He could not speak, and vision was blurred. At that time his physician noted slight right hemiparesis, right hemihypesthesia, right hemiataxia, paresis of the rectus externus muscle of the right eye and slight motor aphasia. The ocular fundi were normal. Serologic examination of the blood and cerebrospinal fluid gave negative results. There were signs of slight arteriosclerosis and arterial hypertension. The state of the patient improved greatly.

Neurologic Examination.—Innervation of the left cheek was weaker than that of the right. The knee jerks were present; the ankle jerks were weak. The left abdominal reflex was weaker than the right. There was ataxia in both legs and in the left arm. There was hypesthesia over the left half of the face. In the left upper limb there was slight paresis with hypertonus.

There were rhythmic twitchings of the palate, the faucial pillar and the posterior wall of the pharynx, all synchronous and unilateral, on the left side. Their rate was about 136 per minute. We did not see any myoclonic movements of the eyes, face, tongue, larynx, intercostal muscles or diaphragm (roentgen examination).

The pulse rate was from 72 to 84 per minute; the arterial pressure was 170 systolic and 80 diastolic.

CONCLUSION

All our cases belong to the group of vascular lesions. In cases 1, 2 and 3 there was arterial hypertension, and the diagnosis of arteriosclerosis was beyond doubt. In case 4 the diagnosis did not seem as certain, but a vascular process was probable in this instance, too. In cases 1, 2 and 3, as in many other recorded cases, the clinical picture was that of pseudobulbar paralysis.

EFFECT OF PLEASANT AND UNPLEASANT IDEAS ON RESPIRATION IN PSYCHONEUROTIC PATIENTS

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The relation between mental phenomena and respiratory function has long been of interest to psychologists and physicians. Many earlier workers, notably Lehmann,[1] Mosso,[2] Mentz,[3] Rehwaldt[4] and Zoneff and Meumann,[5] investigated the effect of various types of ideational stimuli on respiratory tracings in normal persons. More recently, the influence of emotions on respiration and metabolism has been studied by Feleky,[6] Landis[7] and Landis and Gullette[8] in normal persons; by Segal, Binswanger and Strouse[9] in hyperthyroid patients, and by Ziegler and Levine[10] in psychoneurotic patients. There have been

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This is the first in a series of studies on respiration in psychoneurotic patients.

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studies on the effect of emotions on the inspiration-expiration ratio by Mentz,[3] Mosso,[2] Benussi,[11] Burtt,[12] Mignot and Le Grande[13] and Landis and Gullette.[8] Golla and his associates[14] studied various types of respiratory tracings found in schizophrenic patients. Peterson and Jung[15] studied the relationship between respiratory tracings and psychogalvanometric readings on the skin. Christie[16] described various types of respiratory tracings found in the neuroses, and Saul and Alexander[17] attempted to correlate certain aspects of the respiratory curve in psychoneurotic patients with specific personality traits. Many of these investigators studied the respiratory rate alone; others studied only the depth of respiration or the oxygen consumption. In some of the studies the preliminary period was too short to establish a significant base line for individual subjects. Few subjects were used in most of these studies, the largest series being that of Ziegler and Levine,[10] which consisted of 14 psychoneurotic patients and no control subjects.

In an attempt to understand more fully the respiratory function and its well known disturbance in psychoneuroses, and especially in anxiety states, the workers in the psychiatric laboratory of the Massachusetts General Hospital have undertaken a comprehensive study of various aspects of the respiratory function in psychoneurotic patients. In this paper are reported the observations on the rate, amplitude, minute respiratory volume, metabolic rate and the expiratory-inspiratory angle in 41 psychoneurotic patients and 21 control subjects during periods of induced ideational stimulation. Studies on other aspects of the respiratory function are being undertaken and will be reported subsequently.

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TECHNIC

Respiratory data for this study were obtained by means of the Benedict-Roth metabolism apparatus. The patients and control subjects included in this series had already had experience with this apparatus, having had basal metabolic determinations prior to the present tests. At the start of the interview which preceded each test, the subjects, patients and controls alike, were under basal conditions; that is, they had not eaten since the evening meal of the previous day and had been lying in bed for at least one-half hour. During the interview they were asked to state any ideas that came to mind when told to think of "pleasant ideas." The replies were recorded. They were then asked to express any ideas that came to mind when told to think of "unpleasant ideas," and these, too, were recorded. The subjects were then connected with the metabolism apparatus, which was filled with oxygen, a mouth piece and a nose clip being used as in routine metabolism tests.

After a routine test for oxygen leakage had indicated that the apparatus was functioning properly, a six minute record of the respiration was made.[18] The investigator was present, but made no suggestions (preliminary period). This period was followed by a six minute period during which the subject was instructed: "Think of pleasant ideas," or "let pleasant ideas come into your head." The "pleasant period" was followed by another six minute period during which the subject was instructed: "Think of unpleasant ideas," or "let unpleasant ideas come into your head." The "unpleasant period" was followed by a six minute period in which the subject was again asked to "think of pleasant ideas," the "second pleasant period." This period was followed by a six minute period during which the subject was told: "Just relax." During each of the four periods that followed the preliminary period, the instructions were repeated every fifteen or thirty seconds. No specific ideas were suggested in any of these tests. After the final period the subject was disconnected from the metabolism apparatus and was interviewed in an attempt to find out what thoughts were present during the different periods of the test.

The respiratory records were analyzed as follows: Respiratory rate was counted directly. Depth of inspiration was obtained by measuring in millimeters the vertical distance between each trough and the successive peak and converting the values into volumes of gas, expressed in cubic centimeters. Throughout this presentation, depth of inspiration and depth of respiration are used synonymously. The product of depth of inspiration, expressed in liters, and respiratory rate gave the minute respiratory volume, expressed in liters per minute. The rate of oxygen consumption was calculated in the usual way, and is presented as the metabolic rate, in percentages. Because of the ideational stimulation, it cannot be referred to as the basal metabolic rate.

The respiratory curves were also classified in terms of the type of transition occurring between an expiration and the subsequent inspiration, that is, in terms of the angle between the downstroke and the upstroke of the pen, which will be referred to as the expiratory-inspiratory, or E-I, angle. This transition has been referred to as the "expiratory tip" (Saul and Alexander[17]). A superficial

18. During the earlier experiments of this series six minute periods were used in most cases, in order to make the data comparable with those obtained in routine basal metabolism tests. In the remaining experiments of the series the duration of each period was reduced to three minutes. The period used in each case is stated in the tabulated data.

study of the curves showed that when the respiratory rate exceeded 14 per minute, the expiratory-inspiratory angle was always very acute. (The kymograph rate used was 3.1 cm. per minute.) For slower rates of respiration the expiratory-inspiratory angle showed various degrees of obtuseness and frequently was distinctly rounded; there appeared to be no obvious or simple relation between the rate of respiration and the type of expiratory-inspiratory angle. Hence, it seemed desirable to classify the curves obtained in terms of the sharpness of the expiratory-inspiratory angle that occurred. To this end, an arbitrary scale was constructed from the record of a patient who showed great variability in the expiratory-inspiratory angle. Individual sections of an expiration and the subsequent inspiration from the respiratory tracings of this patient were cut out and duplicated on white paper, and these sections were arranged on black paper in the order of increasing obtuseness of the expiratory-inspiratory angle. This chart, with twenty gradations between a very sharp angle (no. 1) and a very obtuse, rounded angle (no. 20), was photographed (fig. 1), and the negative was used as a transparent scale which could be superimposed directly on the respiratory curves to be analyzed. In this way, each expiratory-inspiratory angle in the respiratory tracings could be assigned to its appropriate scale number. It was found that two independent workers could duplicate each other's readings to within 1 scale number. The tracings of each subject were thus analyzed period by period and distribution

Fig. 1.—Scale used for classifying respirations in terms of sharpness or breadth of the expiratory-inspiratory angle.

tables and charts prepared in which were shown the frequency with which the different scale numbers occurred. In order to simplify the charts and tables, the scale numbers were grouped by twos, so that no. 1 included nos. 1 and 2, no. 3 included nos. 3 and 4, no. 5 included nos. 5 and 6, and so on, for ten groups, up to no. 19, which included nos. 19 and 20. Angles broader than no. 20 on the scale were all grouped as no. 21. From these distributions the standard deviation and the mean were calculated in the usual way, the range of error in assigning a value to any angle being assumed to be midway between the preceding and the following value.

DATA

The subjects included 41 psychoneurotic patients and 21 persons used as controls. The patients had been under observation and treatment in the psychiatric ward at the Massachusetts General Hospital, and the diagnoses reported are those made in the hospital. The series consisted of 11 males and 30 females. The ages ranged from 15 to 54. The patients (29 patients—7 males and 22 females) whose conditions were diagnosed as hysteria, phobia or anxiety neurosis on the basis of their predominating symptoms are referred to as group 1. The remaining 12 patients (4 males and 8 females) had conditions diagnosed as hypochondriasis, reactive depression, compulsion neurosis or questionable schizophrenia. These are referred to as group 2.

The control subjects consisted of physicians, social workers and medical students who in a brief preliminary interview disclosed no obvious psychoneurotic

symptoms. They were not subjected to a medical examination. The term "control subjects" thus refers to ambulatory, nonpsychotic, healthy persons who, in contrast to the patients, had no outstanding psychoneurotic symptoms as far as could be determined at one interview. This group consisted of 6 males and 15 females. The ages ranged from 18 to 37.

The data are presented in tables 1 to 16. The general data on the patients, the diagnoses and a summary of the reports during the pleasant and unpleasant periods are presented in table 1. The complete data for respiratory rate, depth, minute respiratory volume, metabolic rate and expiratory-inspiratory angle are presented in tables 2, 5, 8, 11 and 14. Mean values for the groups are given in tables 3, 6, 9, 12 and 15. Summaries of the changes from period to period are shown in tables 4, 7, 10, 13 and 16.

Experiments in 4 illustrative cases are presented in detail.

CASE 5.—A married white man aged 33, a weaver, entered the hospital complaining of pain in the lower part of the abdomen, of three years' duration. In addition, he complained of pain in the right groin, aching in the right leg, pain in the left testis, substernal pain, palpitations and a feeling of constriction. Physical examination showed undernourishment, slightly tortuous retinal vessels, hyperactive reflexes, nystagmoid movements of the eyes, tremor of the fingers and eyelids and cool, moist hands. Laboratory data were essentially normal.

The basal metabolic rates were —13, + 33 and + 28 per cent. A roentgenogram of the chest showed an old tuberculous process. A retrograde pyelogram was normal. The mental status revealed a man of low intelligence, with typical anxiety attacks and anxiety dreams. He had been practicing coitus interruptus. He worried about his finances and his wife's fidelity.

The diagnosis was anxiety neurosis and malnutrition.

Of several tests carried out on this patient, two are referred to in the present study. During the first of these tests the periods lasted six minutes, and during the second test, three minutes. The data from the first test, including the patient's replies when questioned by the investigator after the test, appear as those for patient 5 in the tables and in figures 2, 3 and 4. Figure 2 is the respiratory tracing; figure 3 is a summary chart, showing the rate and depth of respiration, the minute respiratory volume and the metabolic rate, and figure 4 shows the frequency distribution of the expiratory-inspiratory angles in chart form. Figure 5 is the respiratory tracing in the second test on patient 5; the data from this test do not appear in the tables.[19] Figure 6 is an enlargement of the tracing in figure 5, showing the abrupt change in the expiratory-inspiratory angle seen at the moment of transition from the first pleasant to the unpleasant period.

Before the patient was connected with the apparatus he was asked what ideas came to mind when told to think of pleasant ideas. After he had replied, he was asked what ideas came to mind when told to think of unpleasant ideas. His replies were:

Pleasant Ideas.—"I think of the country. A lake near my house. I can look at the far hills from the lake. Being out in a boat alone and away from people."

Unpleasant Ideas.—"Seeing some one get hurt. Getting in a street car and feeling sick. Being downtown with people around me. Being hurried by people."

The patient was then connected with the apparatus and subjected to the routine as described in the section on "technic." When the patient had been disconnected

19. When two or more tests were carried out on a patient, only the first test was included in the tables of the present study.

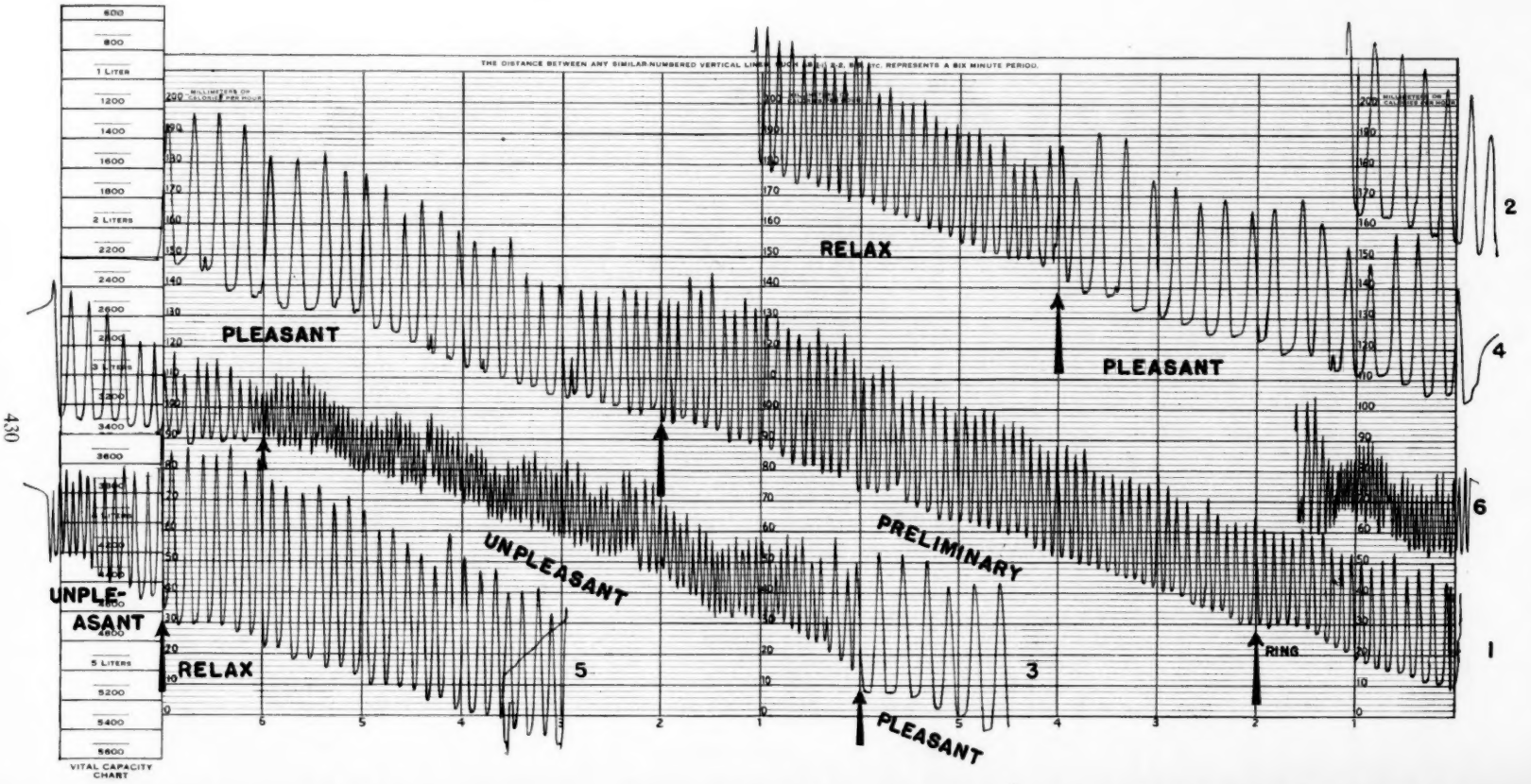

Fig. 2.—Continuous record of a complete experiment on patient 5, with five periods lasting six minutes each. Order in which the tracing is to be followed is indicated by guide numbers *1* to *6* (to be read from right to left).

from the apparatus he was asked to report what he had been thinking during the various periods. His answers were:

Preliminary Period.—"I was thinking of the paper I read, its meaning. Did not have breakfast, read about the ball games. Had visitor yesterday and mentioned going home. Hope these tests will help the doctors. Played cards almost till tea time. Thinking of the test."

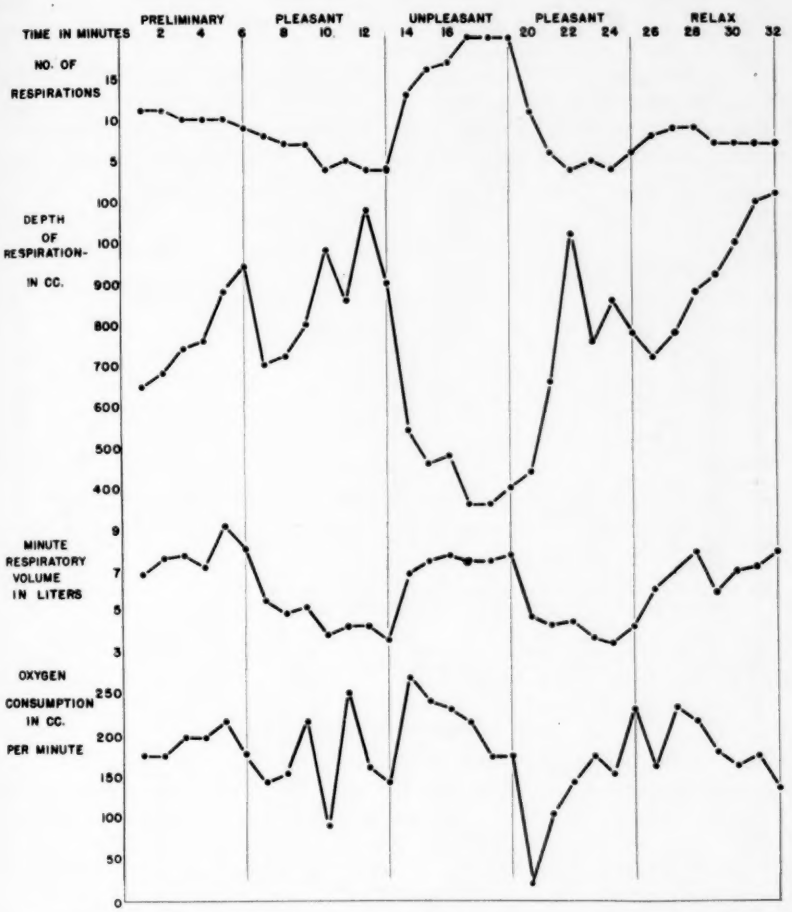

Fig. 3.—Chart showing analysis of figure 2 for rate, mean depth of respiration, minute respiratory volume and oxygen consumption per minute.

First Pleasant Period.—"Lying in the grass; taking a walk in the garden on a warm day; being out on a boat; lying there in the woods. The country always makes me feel quiet."

Unpleasant Period.—"Some one struck by an auto and taken to the hospital. Seeing a crash in the movies. Afraid of being with people. Getting in the street car and feeling of being sick. Don't like crowds."

Second Pleasant Period.—"It took a little time to get back to pleasant ideas. Went back to country near house. Walking in garden, then lying in the grass on a warm day. Same ideas about country come in again."

Relaxed Period.—"Trying to lie here and forget about everybody. Try to let go. Think of sleep, resting completely. Try to rest all the time."

Comment.—The average rate of respiration (patient 5; table 2, fig. 3) was 10 for the preliminary period; it dropped to 6 for the first pleasant period, rose abruptly to 18 for the unpleasant period, returned to 6 for the second pleasant period and was 7 during the relaxed period.

The average value for the depth of inspiration (patient 5; table 5, fig. 3) was 780 cc. for the preliminary period. It rose to 880 cc. in the first pleasant period, fell to half this value, 440 cc., during the unpleasant period, rose again to 780 cc. during the second pleasant period and was 940 cc. during the relaxed period. The

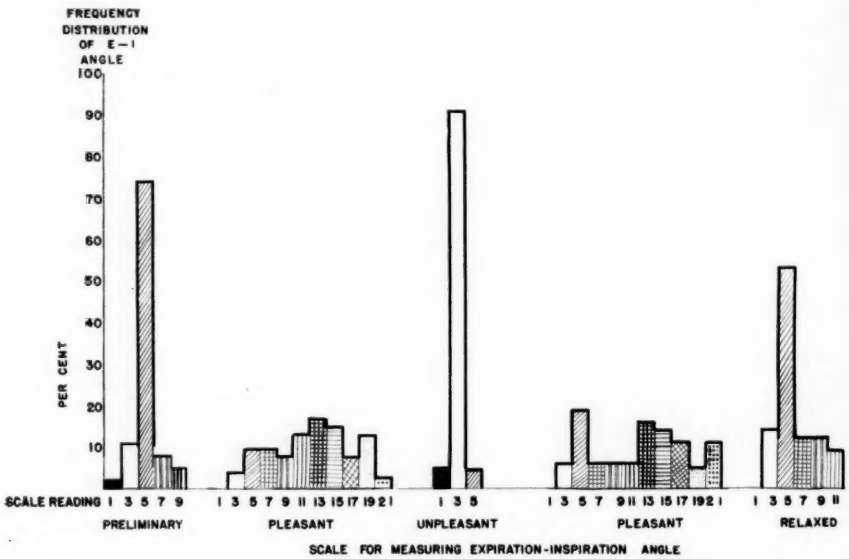

Fig. 4.—Chart showing analysis of figure 2 for frequency distribution of expiratory-inspiratory angles. Group 1 represents scale nos. 1 and 2 combined (see fig. 1); group 3 represents scale nos. 3 and 4, and so on. All expiratory-inspiratory angles broader than scale no. 20 (fig. 1) are given as group 21. The height of the columns indicates the frequency in terms of percentages of the number of respirations occurring during each period.

minute respiratory volume (patient 5; table 7, fig. 3) averaged 8.7 liters per minute during the preliminary period and fell to 4.5 liters per minute during the first pleasant period. During the unpleasant period, for which the average depth of respiration had reached its minimum value, the average minute respiratory volume rose to 7.4 liters per minute. It should be noticed that the increase in minute respiratory volume was effected by an increase in rate, in spite of a decrease in depth. During the second pleasant period the minute respiratory volume fell once more to 4.2 liters per minute. There was a rise to 7 liters per minute for the relaxed period. The metabolic rate (patient 5; table 11, fig. 3) was

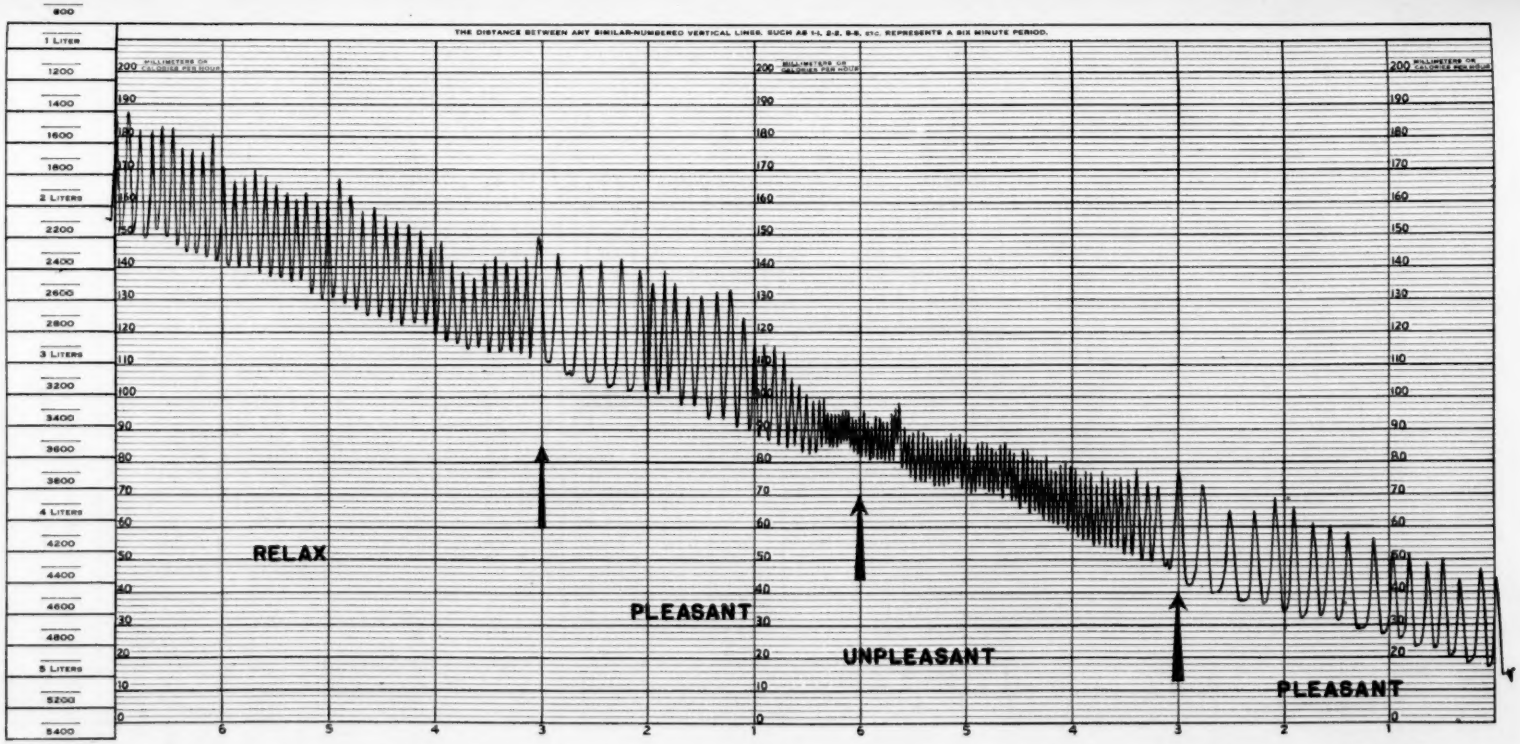
THE DISTANCE BETWEEN ANY SIMILAR-NUMBERED VERTICAL LINES, SUCH AS 1-1, 2-2, 3-3, etc. REPRESENTS A SIX MINUTE PERIOD.
RELAX
PLEASANT
UNPLEASANT
PLEASANT

Fig. 5.—Continuous record of a second experiment on patient 5, to be compared with figure 2. The duration of each period was three minutes. The preliminary period was not recorded.

—1 per cent during the preliminary period. During the three successive periods of ideational stimulation—pleasant, unpleasant and pleasant—it fell successively to —4, —5 and —11 per cent, respectively, and returned to its original value of —1 per cent during the final period of relaxation.

The frequency distribution is shown graphically in figure 4. During the preliminary period the mean expiratory-inspiratory angle was 5.6 (table 14), with a standard deviation of ± 1.4. In other words, the mean expiratory-inspiratory angle fell in the borderline groups in which the rounding of the angle begins to be apparent. The distribution had a rather limited spread. During the first pleasant period the mean shifted to 12.8, with a standard deviation of ± 4.7. The mean expiratory-inspiratory angle was now very broad, and there was a wide spread over the scale.

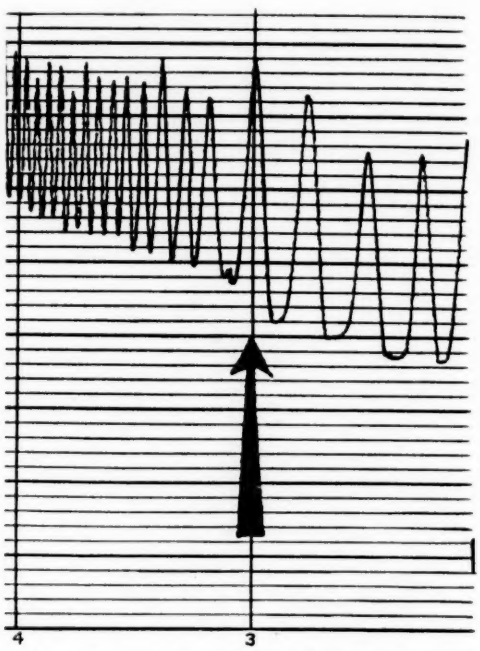

Fig. 6.—Enlarged detail from figure 5, showing the change in the expiratory-inspiratory angle that occurred at the transition from the first pleasant to the unpleasant period.

During the unpleasant period the mean was 3.5, which is a distinctly sharp angle, and the standard deviation was ± 0.6, which indicates that the distribution had a very narrow range. The second pleasant period reproduced closely the picture of the first pleasant period, with a mean angle of 12.6 and a standard deviation of ± 5.6. During the relaxed period the mean angle swung back to 6.5, and the standard deviation, to ± 2.3. The distribution curve for this period resembled somewhat that for the preliminary period, but was slightly displaced toward the more rounded angles.

Case 11.—A white woman aged 31, an unemployed secretary, who was admitted to the medical service for study of high blood pressure and other incapacitating symptoms, complained of nausea, vomiting and irregular menstrual periods for

the past six years. Five years ago, she suffered from sleeplessness, dizzy spells, flashes before her eyes, palpitation and a floating sensation when in bed. She had had an appendectomy at 24 and total hysterectomy and left salpingo-oophorectomy at 29. Among other symptoms, she complained of transient paralysis of the left hand and the legs and hyperalgesia of both hands and feet. She also complained of a feeling of choking and burning in her chest and occasional sensations in her throat. Physical examination revealed the blood pressure to be 190 systolic and 100 diastolic; the retinal arteries were narrow; there were transient tachycardia and palpitations; there was pyuria, with Bacillus coli in the urine. The basal metabolic rate ranged from + 29 to + 8 per cent. Renal function tests showed normal function. A roentgenographic series of the gastrointestinal tract and a barium sulfate enema showed that the constriction was either functional or adhesive. Her mental status showed a marked tendency toward acute emotional outbursts, characterized by palpitation, choking, burning sensations in the throat and considerable worry about the hypertension. Otherwise, the mental status was normal.

The diagnosis was: psychoneurosis, of hysterical type; essential hypertension; adhesions at the rectosigmoid junction.

Three minute periods were used in the test on this patient. Figure 7 is the respiratory tracing made during the test. The average rate and depth of respiration, minute respiratory volume, metabolic rate and the distribution of the expiratory-inspiratory angles are charted in figure 7 and are given in the general tables for patient 11.

The answers before the test were as follows:

Pleasant Ideas.—"Lake; trees; feeling like going under ether; flowers blowing gently; sand; lying down in sand; peace."

Unpleasant Ideas.—"Dying; monster; monster's jaws; sex; feeling hurt; feeling unhappy."

The answers after the test were:

Preliminary Period.—"Had many of these tests before; watching the apparatus bob up and down. Feeling better on the ward. Everybody had a party yesterday, would like to be well and go out again. Letter from father in Maine. Would like to be there for a while."

Pleasant Period.—"Being a little girl in the country; picking violets, picking buttercups; music; music of the soul. Thinking of peace; quiet rhythm; harmony of the soul; church choir; choir boys."

Unpleasant Period.—"My sister and brother-in-law; sister unhappy; once I got mad, packed my clothes and left home for good; tired, weary; girl murdered running into a drugstore."

Pleasant Period.—"Thinking of the beach; lying in the sand on the beach; looking at the water; flowers give me a pleasant feeling. Feel like going under ether."

Relaxed Period.—"Hard to relax; hard to let go; feel cramp in my legs; throbs; hard to let go; tried to relax, but with difficulty."

Comment.—The average rate of respiration (table 2) was 11 per minute for the preliminary period, 10 during the first pleasant period, 11 during the unpleasant period, 9 during the second pleasant period and 12 during the relaxed period. The average depth of respiration (table 5) was 400 cc. during the preliminary period and 440 cc. during the first pleasant period. It increased markedly to 700 cc. during the unpleasant period and fell to 420 cc. during the second pleasant period. During

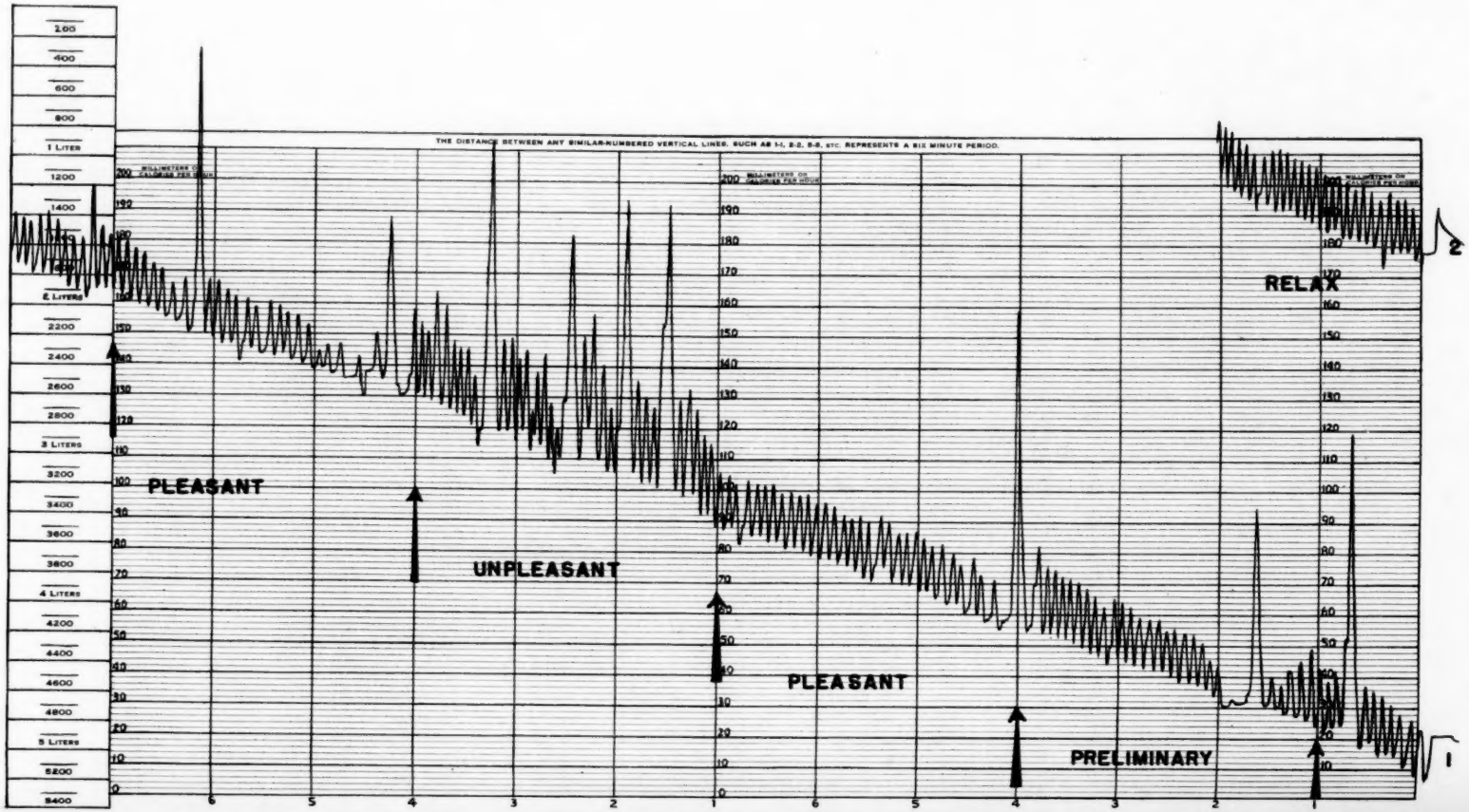

Fig. 7.—Continuous record of an experiment on patient 11. The duration of each period was three minutes.

the relaxed period the average value was 380 cc. The average minute respiratory volume (table 8) was greatest (7.6 liters) during the unpleasant period; the average values, expressed in liters, for the five successive periods were 3.4 (preliminary period), 4.3 (first pleasant period), 7.6 (unpleasant period), 3.6 (second pleasant period) and 4.6 (relaxed period). In this case, in contrast to that of patient 5, an increase in minute respiratory volume during the unpleasant period was produced by deeper breathing, while the rate changed little. The metabolic

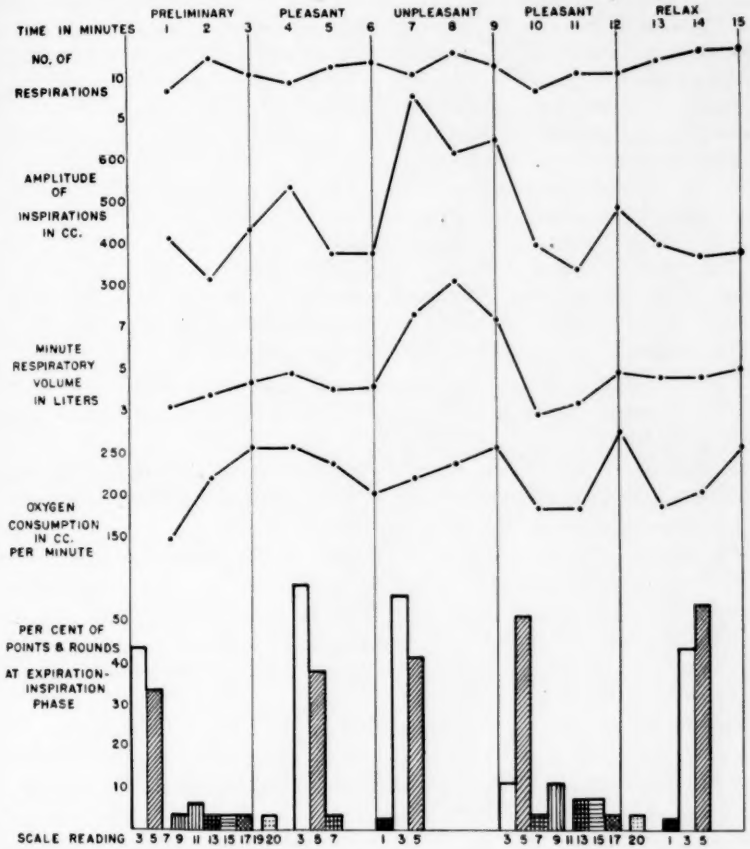

Fig. 8.—Chart showing analysis of figure 7 for rate, mean depth of respiration, minute respiratory volume, oxygen consumption per minute and frequency distribution of the expiratory-inspiratory angles.

rate in this case was somewhat greater during the unpleasant period than during the other periods, the successive values being + 7 per cent (preliminary period), + 14 per cent (first pleasant period), + 23 per cent (unpleasant period), + 4 per cent (second pleasant period) and + 17 per cent (relaxed period). The mean expiratory-inspiratory angles during the five periods were: 6.1, 4.4, 4.3, 8.2 and 4.5, respectively. The greatest change was that from the unpleasant to the second pleasant period, a change from 4.3 to 8.2, or from the borderline between sharp

Fig. 7.—Continuous record of an experiment on patient 11. The duration of each period was three minutes.

and round angles to distinctly round angles. The drop in respiratory rate accompanying this change in the shape of the curve was only from 11 to 9 per minute.

CASE 10.—A married woman aged 26 was admitted with the complaint of abdominal pain, of five years' duration. She also complained of several episodes of vomiting, which showed no special relation to the pain. Her condition had been diagnosed as duodenal ulcer, but in the absence of roentgenographic findings and because of other symptoms, she was transferred to the psychiatric ward. There was a return of the epigastric pain, with nausea, weakness, dizziness and constipation, eight months before. The patient stated that during periods of stress her symptoms were much worse. She also stated that when upset she noticed palpitations and some difficulty in breathing. Physical and neurologic examinations gave essentially normal results. The mental status showed a person with mild emotional swings and definite evidence of fear and anxiety. During the episodes of anxiety there was marked exacerbation of pain. She complained of many aggressive and cruel fantasies and feelings of guilt.

The diagnosis was psychoneurosis, hysteria.

Three minute periods were used in the test on this patient. The respiratory record of the test is shown in figure 9, and the data derived from this record are charted in figure 10. The data also appear in the tables for patient 10.

The answers before the test were:

Pleasant Ideas.—"Being home again; back to work; being home and reading with my little girl; thinking of the country; nice to be near a lake; relaxing; sailboats in the water."

Unpleasant Ideas.—"Being angry at husband at times; husband not wanting me; family difficulties; father always bothers me when he talks about my husband."

The answers after the test were:

Preliminary Period.—"Thinking of things on the ward; making a bag in O. T. [occupational-training]; helped on ward yesterday with a patient; don't mind the tests now; not thinking of anything particular."

First Pleasant Period.—"Nice to be near a lake; sailboats in the water; water plane riding; the country always makes me feel quiet; picture a little house in the country when I am well."

Unpleasant Period.—"Angry at husband when I feel he doesn't care, would like to hurt him; my own family was interrupting always, telling me what to do; feeling upset and worried; jumpy feeling inside. Dizzy feeling and heart pounding."

Second Pleasant Period.—"Thinking of the country most of the time; having a home in the country with my little girl; it's a lake and sailboats gliding on the surface of the lake."

Relaxed Period.—"Trying to be quiet and relax, just like going to sleep; feel heavy in the legs; feel legs on bedclothes; just trying to let go, as you say."

Comment.—It will be seen from figure 9 that there was again a marked increase in minute respiratory volume during the unpleasant period. In this case the increase was effected by increases in both rate and depth of breathing. The metabolic rate was higher during the unpleasant than during the first and second pleasant periods.

The frequency distribution of the expiratory-inspiratory angles is charted in figure 10. The mean values for this angle for the five periods are: 4.9 (preliminary period), 5.4 (first pleasant period), 3.3 (unpleasant period), 5.8 (second

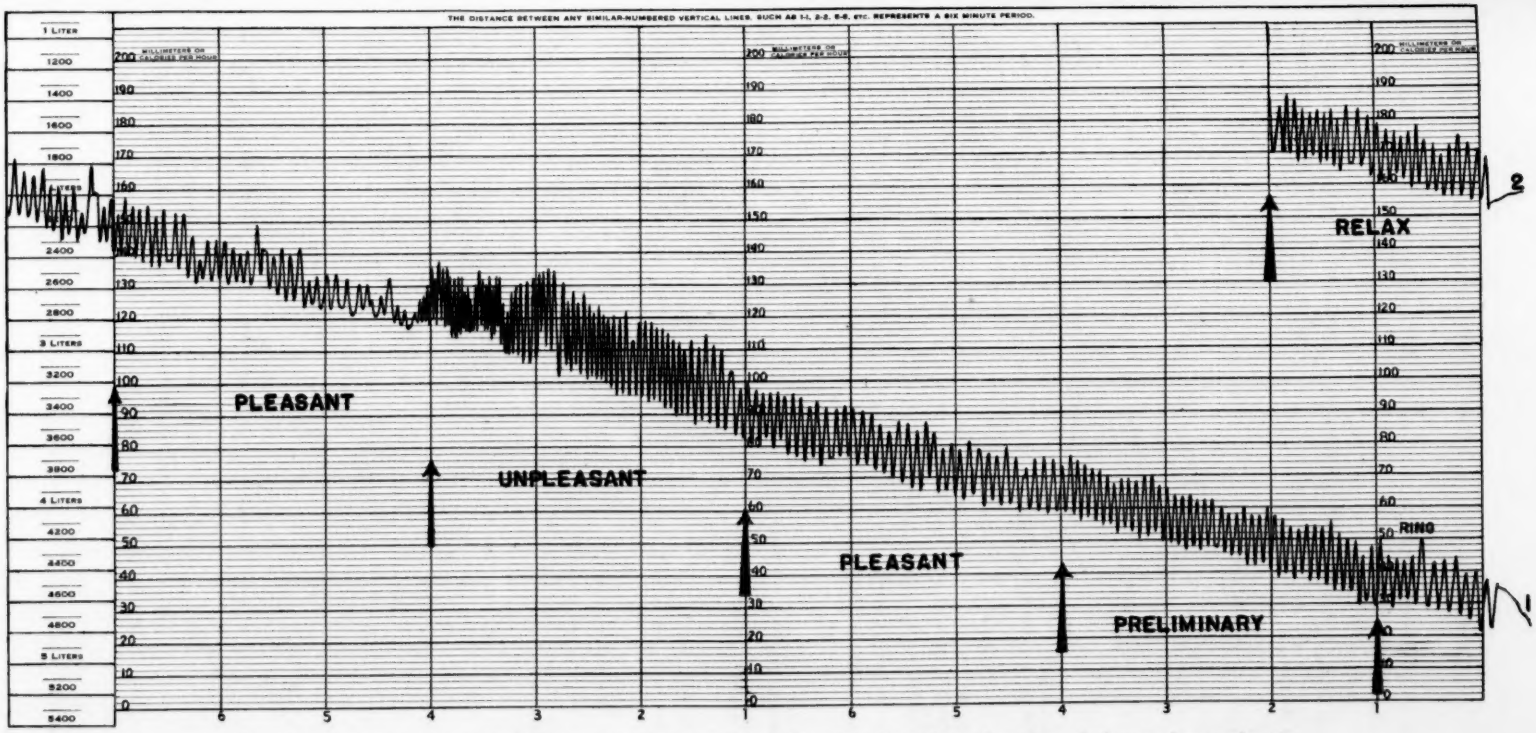

Fig. 9.—Continuous record of an experiment on patient 10. The duration of each period was three minutes.

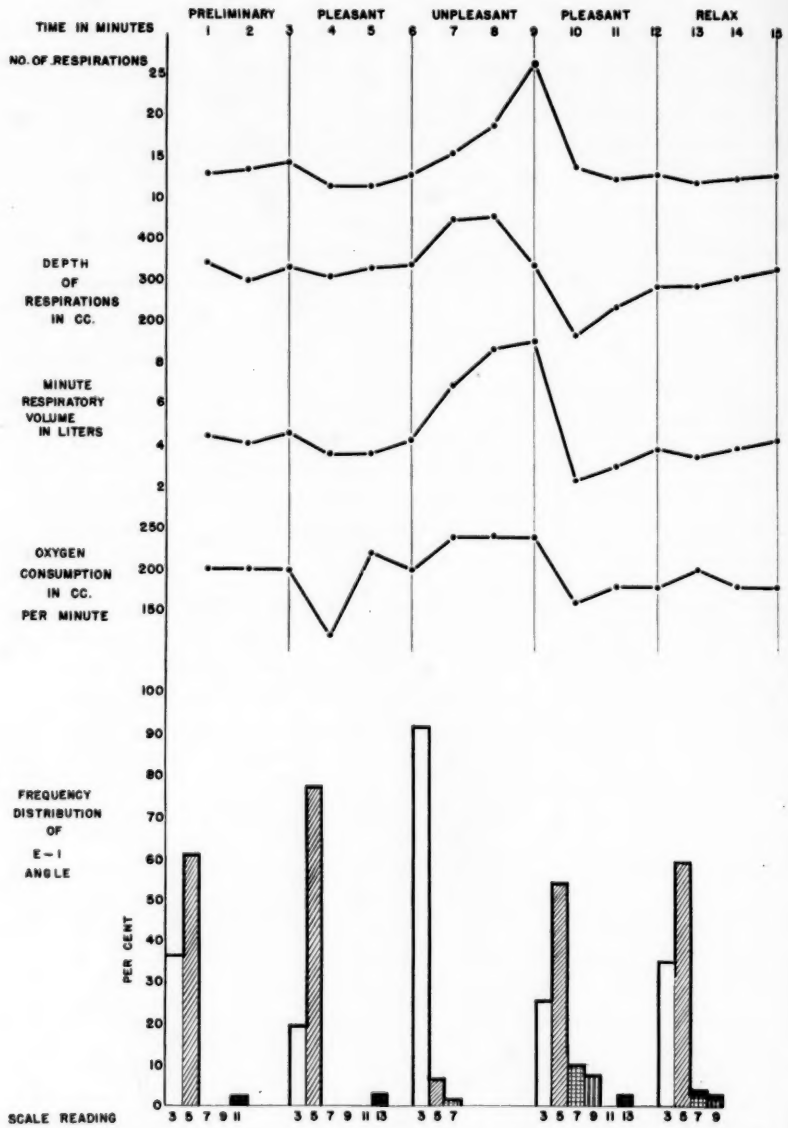

Fig. 10.—Chart showing analysis of figure 9 for rate, mean depth of respiration, minute respiratory volume, oxygen consumption per minute and frequency distribution of the expiratory-inspiratory angles.

pleasant period) and 5 (relaxed period). The mean angle did not shift into the round, broad side of the scale, but it was broadest and had the widest spread (standard deviation, + 2.13) for the second pleasant period, while next in order of breadth of spread was that for the first pleasant period. The usual shift during the unpleasant period to sharper angles in this case accompanied a pronounced rise in respiratory rate.

CASE 12.—A white man aged 27, married, was transferred from the medical service, with the complaint of diarrhea with mucus, of about five years' duration. He complained of difficulty in holding his positions and of apprehension and feelings of guilt. The first appearance of mucus and blood in the stools came after his wife miscarried. After that he worried a great deal about his own illness and that of his wife; at times he complained of anxiety and palpitations, pressure in the head and deep breathing.

The diagnosis was mucous colitis; psychoneurosis, anxiety neurosis.

The respiratory tracing for the test on this patient is given in figure 11. Three minute periods were used. The data are charted in figure 12.

The answers before the test were:

Pleasant Ideas.—"Walking through the woods; sitting in a rowboat; fishing; out for a walk with my wife; building a house; flowers; lying on a beach."

Unpleasant Ideas.—"Falling out of a 40 story window; washing windows up high; picking a fight with my brother-in-law; barber gets insane and cuts my throat."

The answers after the test were:

Preliminary Period.—"Picking up paper this morning and reading about baseball game; talking to Mr. M. about his business; I knew I would have a test and miss breakfast; worked on the grounds yesterday."

First Pleasant Period.—"Woods; singing of birds; picking blueberries; in country with my wife; fishing gives me a quiet feeling; sitting in a boat waiting for fish."

Unpleasant Period.—"Picking a row with a tough fellow makes me mad; feel like a baby; grabbing him by the neck and busting him open; picking a fight with brother-in-law; barber getting insane and cutting my throat makes me most upset."

Second Pleasant Period.—"Fishing in a boat again most pleasant idea; like to sit back and look at boats; looking at flowers."

Relaxed Period.—"Try to forget everything; trying to go to sleep; heavy feelings in legs; trying to let go; just let go of everything."

Comment.—The respiratory tracing for patient 12 shows some similarity to that of patient 11 (fig. 7). Both show fairly uniform breathing at a moderate rate during the preliminary and the first and second pleasant periods, characterized by an occasional deep sigh. Both patients responded to the unpleasant ideas by deep breathing, with little change in rate. The curve for patient 12 is slightly more regular throughout than that for patient 11, and much more so during the unpleasant period. The superficial similarity between the curves becomes more pronounced when one compares figure 12, in which are summarized the data for patient 12, with figure 8, in which are charted the data for patient 11. In contrast with the negligible changes in rate are the striking changes in depth of breathing and minute respiratory volume, which for patient 12 are greater than those for patient 11. In the change from the first pleasant to the unpleasant period, the mean depth of respiration for patient 12 increased by 500 cc., and the minute

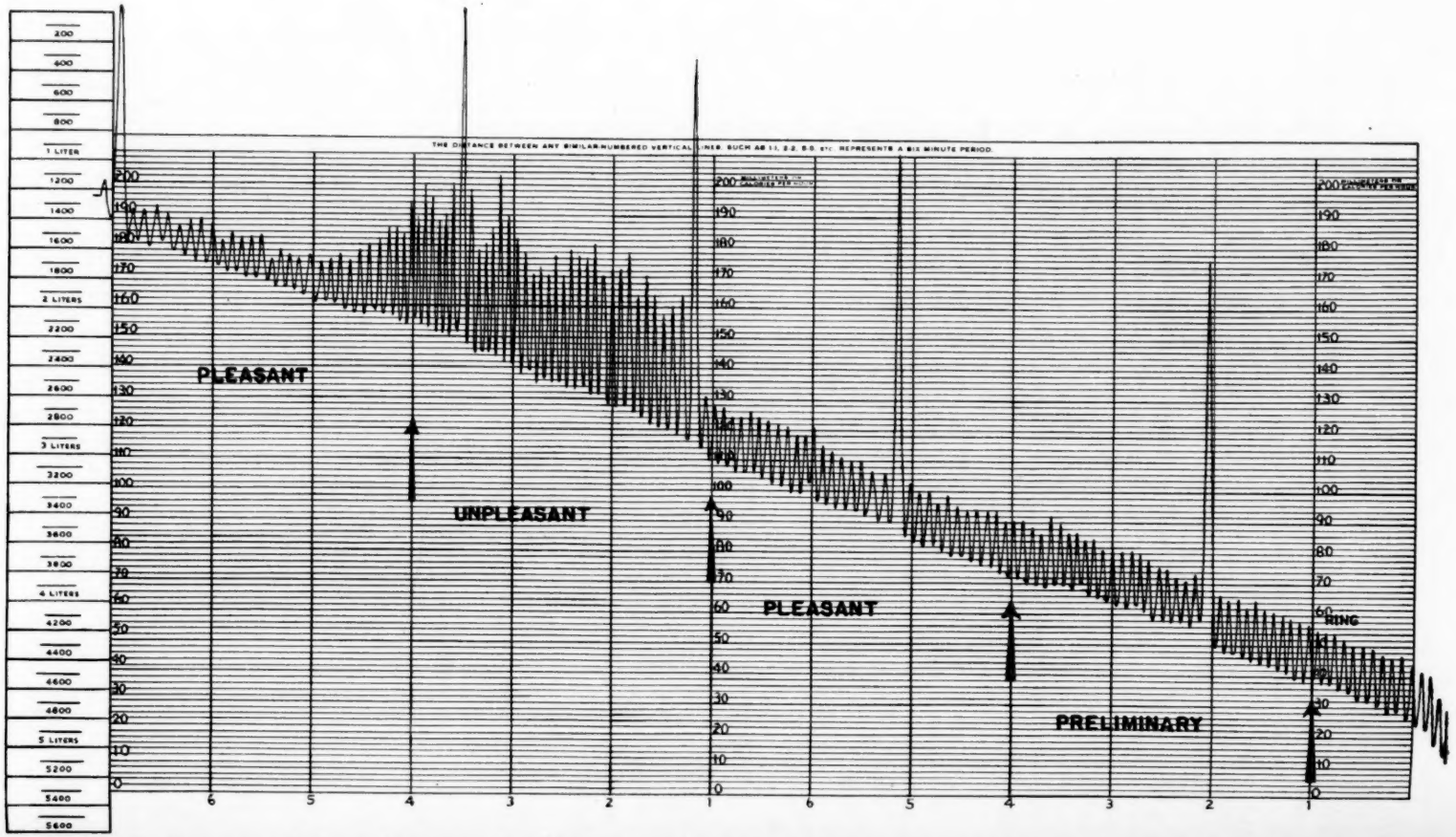

Fig. 11.—Continuous record of experiment on patient 12. The duration of each period was three minutes. The period of relaxation was omitted.

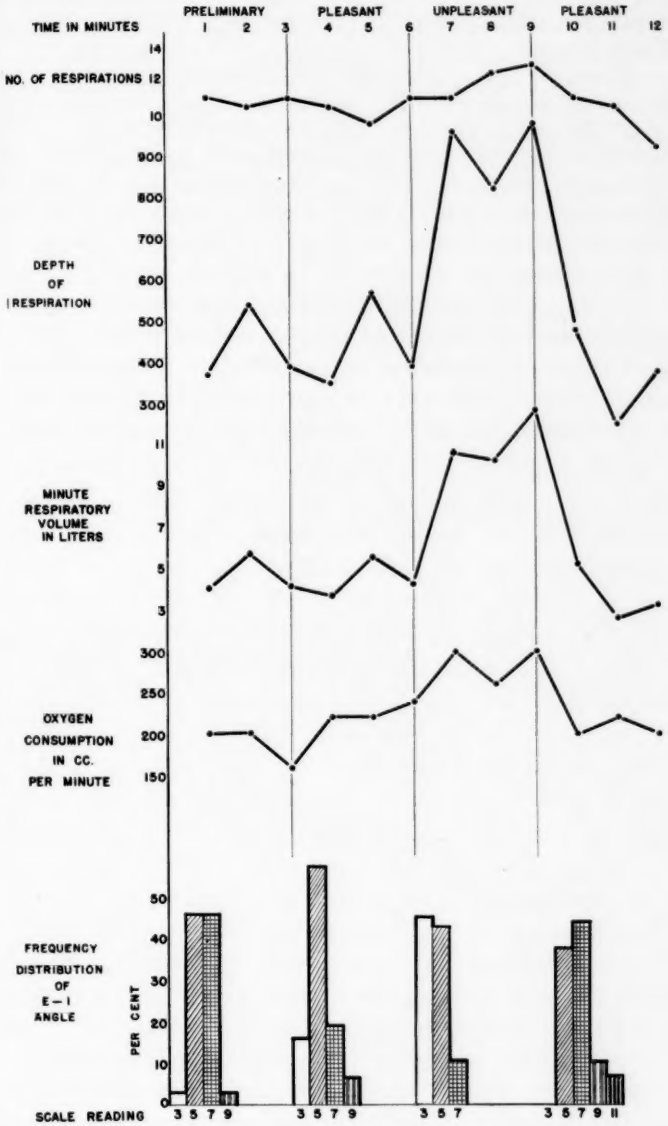

Fig. 12.—Chart showing analysis of figure 11 for rate, mean depth of respiration, minute respiratory volume, oxygen consumption per minute and frequency distribution of expiratory-inspiratory angles.

Fig. 11.—Continuous record of experiment on patient 12. The duration of each period was three minutes. The period of relaxation was omitted.

respiratory volume, by 6.7 liters. The decrease from the unpleasant to the second pleasant period was 560 cc. for the mean depth of respiration and 7.8 liters for the minute respiratory volume. The metabolic rate for patient 12 rose during the unpleasant period.

The frequency distribution of the expiratory-inspiratory angles (fig. 12) reflects the general uniformity shown in the respiratory tracing of this patient for any given period. The spread of the curve in every case is rather limited, and at least 40 per cent of the angles in each period correspond to nos. 5 and 6 of the scale. The mean expiratory-inspiratory angle for the unpleasant period is 4.8, which is only slightly sharper than that for the first pleasant period. There is a shift to 7.4 for the second pleasant period.

IDEAS REPORTED

Pleasant Ideas.—A survey of table 1 indicates that most of the subjects responded to the suggestion to think of pleasant things with a uniform ideational content.[20] Of the 41 patients, 22 reported having thought of rural scenes and water scenes; 8 thought of rural scenes without mentioning water, and 6 spoke of water without any reference to rural scenes, making a total of 36 patients having pleasant ideas associated with country scenes, with water scenes or with both. Of the 5 patients who did not express ideas about the country or water, 4 were concerned with children or babies and the fifth with being at home. Of the whole group, 6 referred to music, 4 to reading, and 3 to church; only 3 mentioned thinking about being well or getting better. The ideas associated with the country were mainly of trees, woods, walking in the woods and lying under trees. The ideas connected with water were chiefly of looking at lakes or at the ocean, of lying on the beach, of looking at boats and of fishing. These ideas seemed to be associated with the idea of vacation. Individual variations were conspicuously absent. Occasionally a particular spot in the country was referred to, or a given trip or piece of music was mentioned by name. The only really individual pleasant idea reported was that of a man who referred to studying mechanics of boats. In almost every case the pleasant ideas were associated with physical inactivity, such as lying on the beach, looking at lakes, fishing or listening to music. There were no reports of active ideas (other than of walking or boating) and none of erotic ideas. The feeling tone throughout was one of peace, quiet and restfulness. Strictly speaking, the feeling during the pleasant periods as indicated by the reports, as well as by the general demeanor of the patients, can best be described by such qualifying adjectives as "peaceful," "restful," "quiet," "relaxing" and "inactive."

20. The pleasant ideas reported in table 1 were collected from the first and the second pleasant period.

There was little difference between the reports for the two pleasant periods in any given case. Some patients reported, however, that they were unable to revert to pleasant ideas at once after the unpleasant period (cases 5 and 22). Two patients (cases 7 and 36) reported that they were unable to let pleasant thoughts come to mind at all during the second pleasant period.

The pleasant ideas reported by the control subjects were similar to those described by the patients. In every case reference was made to rural scenes, to water scenes (including boats) or to both. Three controls reported, in addition, thoughts of home, and 4 mentioned babies (1 of these, a man, referred to relief after the birth of his child). Cultural subjects, such as music and poetry, were mentioned in 5 cases, and food and nice clothes, in 3 cases. Of the 5 controls who referred to some form of activity, all but 1 specified mild forms of activity, such as walking, canoeing, knitting or playing the piano, in contrast to the single subject (no. 7) who referred to tennis and dancing. There was no mention of erotic ideas, nor, with the possible exception of subject 7, were any other stimulating or exciting ideas reported. As in the case of the patients, the feeling tone was one of peace and restfulness.

Unpleasant Ideas.—The unpleasant ideas reported by the subjects were less uniform than were the pleasant ones. The unpleasant ideas can be classified roughly as worries, fears and phobias; memories or fantasies of a cruel or violent nature; ideas concerned with personal ill health and somatic complaints, and a group of lesser problems which can be referred to as annoyances or aggravations. References to fear seemed about equally prevalent among the patients of groups 1 and 2, occurring in about one-half the cases. In group 1 these include 4 phobias (trains, street cars, crowds and closed rooms). Except for a few cases of worries about jobs, most of the remaining fears were concerned with sickness and dying. Group 2 included 1 case of phobia, 3 cases of fear of sickness or dying and 3 cases of worrying about jobs. There was a larger proportion of fears and worries for the control subjects (17 cases). In 7 of these the worries were concerned with jobs or studies; in 4 with sickness or death in the family; in 1 of dying; in 3, with driving on "skiddy" roads; in 2 there were fears of objects. With 1 possible exception (fear of a rat), none of the fears reported by the control subjects had the character of a phobia, and most were concerned with current, real problems.

Cruel and aggressive ideas (anger, operations, accidents, cruel fantasies) were reported by 15 patients of group 1, by 5 patients of group 2 and by 9 control subjects. Thoughts of automobile accidents, operations and deaths occurred with almost equal relative frequency for all patients, namely, four times for group 1, twice for group 2 and five times for

TABLE 1.—*General Data on Patients and Control Subjects, with a Summary of "Pleasant" and "Unpleasant" Ideas*

No.	Sex	Age, Yr.	Ideas in Mind During Pleasant Period	Ideas in Mind During Unpleasant Period	Diagnosis
			Patients		
1	F	26	Lake; rock; sitting near rock; reflection in lake.....	Husband; unexpected things happening to me; problem about babies	Anxiety neurosis; malnutrition
2	F	33	Reading in front of fireplace; trip to Canada six years go; lying under tree in garden	Attack of anxiety last night; feeling that I'd die; heart running wild	Hysteria; bromidism
3	F	23	Sunday morning at church; organ music at church; looking at country and lake	Husband unfaithful; patient operated on head; can't get back to baby	Anxiety neurosis
4	F	37	Nice ride; spending quiet evenings at home; visiting country; visiting beach	Sick; fire alarm; being here in hospital; need for operation	Anxiety neurosis
5	M	33	Lying in grass; walking in garden; being out on a boat; lying in woods	Some one getting hurt, struck by an automobile; crash; afraid of being with people	Anxiety neurosis; malnutrition
6	F	36	Furnishing my home; resting in country; hammock in daughter's house; lying under tree	Sickness; thinking my girl was mean to me; that made me cry; feeling desperate	Hysteria
7	F	30	Pretty home; children dressed nicely; talented; concert in flower garden; "Flight of Bumble Bee"	Frightened at having a child; bill collectors; couldn't stand baby crying	Anxiety neurosis
8	M	31	Maine last fall; woods and lakes in New York; being at home; songs; "Liebestraum"	Things happening at home; experience with man; masturbation and after-effect	Anxiety neurosis
9	F	31	Children well cared for; calm feeling when things run smoothly; working quietly	Sickness; worry about bills; husband used to drink; I hated him	Anxiety neurosis
10	F	26	Nice to be at lake; relaxing; sailboats; water; pleasant country	Angry at father; husband not wanting me; angry at his family	Hysteria
11	F	31	Lake; trees; feeling like going under ether; flowers; blowing gently; lying in sand; peace	Left home for good; dying; monster's jaws; feeling hurt; feeling unhappy; girl murdered running into drugstore	Hysteria; essential hypertension
12	M	27	Walking through woods; sitting in rowboat; fishing; birds singing in woods; picking blueberries	Falling out of a 40 story window; barber gets insane and cuts my throat; fight with fellow; busting him open	Anxiety neurosis; mucous colitis
13	F	23	Free from worrying; out in country; lakes; woods; swimming; work with no friction	Inability to make plans; being at home and sick; being disgusted; this continuous mess	Anxiety neurosis
14	F	32	Country; several trips in country; last trip to Bermuda.....	Plans not going well; working up into a temper; thinking about my sickness	Hysteria
15	M	42	Fishing in Maine; swimming at night at F.; lying on a float near shore	Riding on street car and fainting; fear of walking alone to hospital; feeling helpless	Anxiety neurosis; phobias
16	M	21	Fishing; waiting for a bite; lying on seashore; lying in woods, under nine trees	Stomach trouble; belching; heart terrible; fear of dying; fear of being sick	Anxiety neurosis; (?) reactive depression
17	F	18	Scenes on farm; being with family; country; walks; lakes	Worrying my mother; making her most unhappy; things I haven't been able to do	Hysteria
18	F	24	Lying under tree reading; summer vacation in mountains; relaxing on shore	Experience of being forced by man; feeling upset when mother questioned me about man	Hysteria
19	F	29	Baby snuggling up close; working along at home.....	Death of my mother; something happening to baby; many problems	Anxiety neurosis; phobias
20	F	54	Flowers; trees; blue skies in Jamaica; beautiful gardens; birds singing	being dominated; not able to open windows; fear of water; shut in room	Hysteria; mucous colitis

			Being in woods; Franklin Park; looking at lake in woods;	Being stabbed in left side; feeling that I have to fight some	Anxiety neurosis

			birds singing	shut in room	Hysteria; mucous colitis
21	M	28	Being in woods; Franklin Park; looking at lake in woods; feeling completely well	Being stabbed in left side; feeling that I have to fight some one; stepmother's treatment of me	Anxiety neurosis
22	M	38	Walking on pavement; in garden; country with trees and flowers	Being sick; heart fast; I have a cancer and am going to die	Anxiety neurosis, hysterical features
23	F	23	Pleasant boat trip; being on boat and looking at the water	Losing my job; being here in hospital; feeling I will not get well	Hysteria
24	F	19	Boat trip; reading nice story; goin for walk in country	Getting up to recite; concentrating at desk; feeling not able to do it; chemistry	Anxiety neurosis
25	F	26	Vacation near Lake S.; lying in canoe toward evening; sleeping out at night	Seeing auto accident; man lying in road; scolded by older sister	Hysteria, with anxiety features
26	F	22	Boating; woods; walking on boat; music; walk in rain.....	Being in a crowd; having a lumbar puncture; running into stepfather	Hysteria
27	F	26	Seashore; country scene; lakes; being married; having a home	Unpleasant operation; not being able to walk; being cut open	Anxiety neurosis; malignant hypertension; syphilis
28	F	24	Reading; theater; travel; flowers; nice clothes; vacation in country; grass with flowers	Being sick; dying; accidents; quarreling with people; death	Anxiety neurosis; phobias
29	F	31	Home just after we were married; meeting obligations; walking near summer place	Idea of choking at night; fear of having another baby; not getting well	Hysteria; bronchial asthma
30	F	37	Being at home; resting and relaxing at home.....	Being sick; just dying in bathroom.....	Hypochondriasis; reactive depression; involutional melancholia (?)
31	F	30	Walking in woods; trying to sleep; resting under a tree in the summertime	I can't get help; Bob is dead; can't get well again.....	Reactive depression; hypochondriasis; psychopathic personality
32	M	42	Feeling I'm getting well; woods and lakes; walking alone under trees	Feeling of not making the grade; difficulty in getting work; lack of concentration	Hypochondriasis; compulsion neurosis
33	F	16	Water; Charles river; trees; country; scenery in country; on beach reading a book	Riding in a train; feel dizzy in sun; afraid of people; "scary" feeling in hot room	Psychoneurosis, mixed type; (?) schizophrenia
34	F	17	Old-fashioned garden; lying under a tree; quiet and peaceful church in New York; lake near Marlborough	My aunt she tried to put me in psychopathic hospital; death of mother	Reactive depression; hypochondriasis
35	F	31	Trip on boat; train after boat; autumn leaves and colors; snow; pleasant times before marriage	Husband bothering me; husband's folks upsetting me; being sick this way	Hypochondriasis, with depressive features
36	F	23	Good movie; singing; sleeping; church; country; skating; trees and woods	Sickness; hard time finding work; fighting with girl; being nagged	Reactive depression; hypochondriasis
37	F	27	Thinking of going to sleep; baby asleep; unpleasant ideas pushes them out	Things to be done; not able to do them; too much to take care of; house and baby	Reactive depression; old abscess of lung
38	M	33	Fly casting; fishing; hunting with boys; getting over this dizziness	Trying to fight off symptoms; thinking of Joe, who was operated on; operation on skull for blood clot; scar in brain	Hypochondriasis; (?) multiple sclerosis
39	F	26	People singing; travel; trip to Europe; Lohengrin; reading books; pleasant weather	Any idea of nervousness; having the blues; not getting over this trouble; hospital with many patients	Hypochondriasis; (?) chronic encephalitis
40	M	51	Lying down; picnic; going out in the country; looking out at the sea	Ideas of headache; sickness makes me feel upset; being on relief; something makes me suffer	Compulsion neurosis; hypochondriasis
41	M	30	Sailboats; watching boats from the beach; studying mechanics of boats	Work; sickness; cruelty; irritating people; nervous condition; working with tough person	Hypochondriasis

TABLE 1.—*General Data on Patients and Control Subjects, with a Summary of "Pleasant" and "Unpleasant" Ideas—Continued*

No.	Sex	Age, Yr.	Ideas in Mind During Pleasant Period	Ideas in Mind During Unpleasant Period
			Control Subjects	
1	M	32	Quiet, peace; good job; companionship of people; woods; particular spot in the country; trip to New York	Sick, not being in good health; without job, wife sick; ill luck in business affairs; things I should have done differently
2	M	19	Motoring slowly; walking in woods; being out in open	Brother's illness, sister-in-law nasty, not understanding; frightened at night by a "drunk"
3	F	23	Looking over side of big boat; canoeing at sunset, walking through woods; symphony concert; having and holding my own baby	Not getting a job. What will family say? How shall we manage? Family rejection of me; family discord, husband vs. mother
4	F	29	Woods, hills and mountains; canoe drifting down river; turtles on log; looking at sunset on Mount W.	Being late for dentist; waiting for people; driving a car on snow and ice; skidding while driving an automobile
5	F	23	Country; shore; sleeping; rural scenes; lying down on shore; open country, water, clouds	Having to talk before people; scrapping with people; auto accident, some one killed
6	F	25	Nice places to go; West Indies; good quiet places, no people around; just want husband, no one else; nice clothes; music; white clean farmhouse	European situation; Fascists; floods; girl I don't like; politics and details of political deals; things I'm "griped" at
7	F	27	Food; sleep; tennis; dancing; scenery; Lake Como; water lapping on shore; sunshine; sky colors I like	War in Europe, Spain; cruelty, sadism, being hurt; when you're feeling helpless; slow murder; people who have done me dirt
8	F	30	Lying on beach in sun, sailing, canoeing; sitting in front of fireplace; brook	Skidding in car on ice; driving on icy road; mostly consequences of skidding in car; accident
9	F	29	Sun and sand; want to be out on sand getting sunburnt; beach; having a child	Menstruation; household responsibilities; things I have failed in; ideas that people do not like me
10	M	34	Lying under a tree and looking into sky; boat far out in ocean; spring air	Guilt feelings, not having been fair to best friend; rat in the room
11	M	30	Sitting in a deck chair; boat trip; relaxing in warm sun on deck	Anger at mother, arguments with father; driving in rainy weather; angry at family
12	F	18	Country in Maine; summer in the mountains; feel easy on a clear, warm day, on lake in mountains	Hurt by my friends; hate to talk before a group; examinations I've not prepared for; war and misery
13	F	31	Sitting on lower part of boat; lying in deck chair; lying on back after swimming	Aggravating situation with friend, upset for several days; news photos of war in China
14	F	31	Baby; nice things I do around the house with baby; down at the farm; scenes on the farm	Hurrying things; certain kinds of housework; tiff with sisters
15	F	37	Trees; cool things; woods; lakes; grass; food; home.....	All kinds of messes; noisy things; worry about mother; illness; her death would upset me
16	M	24	Soft music; open fields with a book; wind-swept hill; book of sonnets; boating	Courses I don't like; feel upset at exams; fighting; pushing through crowds; people; to get ahead
17	M	29	Easy feeling after baby was born; woods, country, steamer, coming back from England; deck chair	Tension about birth of baby; business courses at college; ran over dog; owner angry at me
18	F	33	Top of mountain, sitting and talking on mountain; boat riding; sailing around harbor	
19	F	26	Home; country; being with mother; on vacation; open fields	Upsetting family by going off; hurting friend; unjustly accused at school
20	F	23	Mountains; classical music; knitting; playing piano.....	Ideas of death, drowning; mother upset; grandmother nervous
21	F	19	Sunshine, warmth, open fire; beach in the summer, looking at the sea	Feeling that I'm not doing well, would lose my job as a result of my inefficiency; would be tough

the control group. A reference to anger or hatred on the part of the patients appeared twice for each group. Cruel fantasies ("barber goes insane and cuts my throat"; "slow murder"; "monster's jaws") occurred most frequently for group 1 (9 patients). Only 1 such fantasy was reported by the patients of group 2, and 2 were mentioned by the control subjects. Ideas of sickness and somatic complaints (headache, dizziness, stomach trouble, heart beating fast) seemed to be most prevalent for group 2. Ideas of this type were referred to by about one third of the patients of group 1, by over one half of the patients of group 2 and by only 2 of the control subjects. There were references to petty annoyances and aggravations by 9 of the control subjects.

On the whole, the responses of the patients for the unpleasant period were directly connected with their individual problems and symptoms. The ideas reported by the controls were in general of a milder character and in keeping with less intense personal problems. The controls referred more to realistic, current, everyday problems and less to bizarre fantasies (group 1) or to despondency about ill health (group 2). There were many more references to minor annoyances and aggravations.

The reports for the unpleasant period were more strongly colored emotionally than were those for the pleasant period. The feelings reported varied over a wide range, including annoyance, dejection, fear, anger, guilt, sadness and cruelty. Some of the patients showed intense emotional disturbance by restlessness, by facial expression and, in 2 cases, even by weeping. Even the controls seemed much more restless and disturbed than during the pleasant periods, and 1 of them (subject 5) wept during the unpleasant period. From the nature of the responses, it seems reasonable to qualify the term "unpleasant" by such adjectives as "disturbing" or "upsetting."

The ideas reported by the patients for the preliminary period were concerned with relatively casual topics, such as activities in the hospital ward, working in the occupational therapy department or helping in the ward, and included neutral remarks about other patients, comments on the newspapers and noticing apparatus during the tests. The ideas concerned mostly recent events and involved a certain amount of activity. In both these respects this period differed from the pleasant period, which concerned largely memories or imagined scenes and in which there was little mention of any form of activity. The reports of the control subjects for this period concerned similar topics. The subjects, patients and controls alike, did not describe any feelings of anxiety about the tests, but sometimes made passing remarks about the apparatus, with which they had had experience in previous tests. The ideas reported seemed unconnected with any special emotional tone, and in this particular likewise contrasted with the peaceful, quiet tone of the pleasant period and with the disturbing, upsetting tone of the unpleasant period.

21 F 19 Sunshine, warmth, open fire; beach in the summer, looking at the sea ..... Ideas of death, drowning; mother upset; grandmother nervous ..... Feeling that I'm not doing well, would lose my job as a result of my inefficiency; would be tough

With a few patients short tests were carried out after the usual experiments, during which specific neutral topics were suggested, such as reading the newspaper, sitting on a porch and nonsense syllables. This was done in order to compare the respiratory curves obtained during suggestions of this sort with those for the usual preliminary period.

During the relaxed period most of the subjects reported that they were trying to "let go." Typical ideas reported were: "head touching the pillows"; "feelings of legs and heels touching the bedclothes"; "trying to let go"; "feeling of a hand flat on the bedclothes." A few reported that they were unable to relax.

The investigator had anticipated greater difficulty than he encountered in inducing the desired type of subjective material for the successive periods. The specificity of the ideas reported for each period by the 41 patients and 21 control subjects showed a surprising degree of cooperation on their part. None of the subjects were told of the object of the tests. It should be recalled, furthermore, that with the exception of a few special tests on material for the preliminary period carried out independently, no actual suggestion of content was made by the investigator, who merely repeated: "Think of pleasant ideas"; "let pleasant ideas come into your mind," or "think of unpleasant ideas" and "let unpleasant ideas come into your mind."

RATE OF RESPIRATION

The average rates of respiration found for each of the 41 patients and 21 control subjects during the successive periods are given in table 2. The rates for the patients of group 1 ranged from 6 to 37 respirations per minute, for the patients of group 2 from 6 to 22 respirations per minute and for the control subjects from 5 to 21 respirations per minute. In table 3 and in figure 13 are shown the mean values of these rates period by period, derived separately for all patients, for the patients of group 1 (patients 1 to 29), for the patients of group 2 (patients 30 to 41) and for the controls.

The changes in rate for the successive periods were closely parallel for all the patients taken as a group, for the patients of group 1 and for the controls. During the first pleasant period the rate was similar to, or somewhat less than, the rate for the preliminary period. The rate reached a maximum during the unpleasant period, returned in the second pleasant period to a value close to, or equal to, that of the first pleasant period and decreased to a minimum during the relaxed period. For each period the mean rate for the controls was slower by 2 or 3 respirations per minute than the corresponding mean rate for the patients of group 1, and was slower by 2 respirations per minute than the mean value for all the patients. The mean rates for group 1 alone were similar to those of all the patients taken together, except that in the case of group 1 there was a more pronounced rise during the unpleasant period. This similarity is deceptive and holds merely because group 1 comprised almost three fourths

TABLE 2.—*Average Rate of Respiration Per Minute for Each Period*

No.	Preliminary Period		First Pleasant Period		Unpleasant Period		Second Pleasant Period		Relaxed Period	
	Duration of Period, Min.	Average Rate per Min.	Duration of Period, Min.	Average Rate per Min.	Duration of Period, Min.	Average Rate per Min.	Duration of Period, Min.	Average Rate per Min.	Duration of Period, Min.	Average Rate per Min.
					Patients					
1	7	13	6	14	6	16	..	..	..	..
2	..	..	9	15	6	15	5	13	..	..
3	6	22	7	24	5	24	6	23	8	18
4	..	..	7	14	7	24	8	14	5	13
5	6	10	6	6	6	18	6	6	6	7
6	..	..	6	16	6	18	6	16	6	17
7	6	12	8	12	7	10	6	8	6	8
8	6	15	6	8	7	14	7	11	7	10
9	6	14	6	16	7	12	10	12	2	10
10	3	14	3	12	3	21	3	13	3	13
11	2	11	2	10	2	11	2	9	3	12
12	3	11	3	10	3	12	3	10	..	..
13	3	22	3	20	3	25	3	22	3	24
14	3	12	3	9	3	11	3	10	3	9
15	3	7	3	9	3	9	3	7	3	8
16	6	21	7	22	6	25	6	23	6	19
17	3	30	3	33	3	37	3	35	..	..
18	3	23	3	17	3	22	..	..	..	..
19	3	15	3	15	3	15	..	..	..	..
20	6	15	3	15	3	17	3	15	..	..
21	3	9	3	6	2	11	..	..	..	..
22	3	18	3	21	3	24	3	23	3	24
23	3	16	3	19	3	16	..	..	..	..
24	3	13	3	14	3	16	3	16	3	16
25	3	9	3	11	3	12	3	6	3	7
26	3	16	3	15	3	21	..	..	..	..
27	3	13	..	..	3	16	3	16	..	..
28	3	13	..	..	3	12	3	12	..	..
29	3	16	3	17	3	17	..	..	..	..
30	6	15	3	12	3	15	3	10	3	9
31	3	12	..	..	3	11	3	12	..	..
32	6	11	6	13	6	16	7	13	6	15
33	6	18	6	19	6	19	6	19	6	19
34	6	22	8	17	6	19	6	17	6	19
35	6	10	8	9	6	10	7	9	6	9
36	6	19	6	19	7	15	5	18	6	18
37	6	15	6	15	6	15	7	14	6	14
38	6	14	6	16	6	13	6	16	6	17
39	6	20	7	19	7	19	6	21	2	18
40	6	11	6	13	9	13	6	12	6	11
41	3	9	3	8	3	9	3	8	3	6
					Control Subjects					
1	6	13	6	11	6	11	7	11	7	10
2	3	13	3	13	4	13	4	13	4	12
3	6	15	6	16	6	21	6	21	3	20
4	6	14	6	14	5	15	2	16	9	12
5	6	12	7	10	6	15	6	9	6	11
6	6	12	6	12	6	18	6	13	6	12
7	6	14	12	12	6	17	..	..	7	14
8	3	14	3	12	3	14	3	14	3	14
9	3	12	3	11	3	15	3	13	3	8
10	6	7	6	7	6	9	6	6	6	5
11	3	17	3	16	3	17	..	..	..	..
12	3	15	..	..	3	12	3	14	..	..
13	3	15	3	14	3	16	3	14	3	14
14	3	12	3	11	3	13	3	12	3	11
15	3	9	..	..	3	10	3	10	..	..
16	3	16	3	17	3	16	..	..	..	..
17	3	14	3	13	3	17	..	..	..	..
18	3	15	3	13	..	..	..	..	..	..
19	3	15	3	15	3	17	3	13	3	13
20	3	8	3	7	3	9	3	7	3	8
21	3	12	3	12	3	15	3	13	3	11

of all the patients tested. The patients of group 2 actually were in marked contrast with the patients of group 1 and with the controls, since the mean rate of respiration for group 2 showed little change during the five periods and no acceleration during the unpleasant period was seen for this group of patients.

TABLE 3.—*Mean Rate of Respiration Per Minute During Each Period*

Group	Number	Preliminary Period	First Pleasant Period	Unpleasant Period	Second Pleasant Period	Relaxed Period
All patients	41	14.8	14.7	16.5	14.4	13.8
Patients, group 1	29	15.0	14.8	17.3	14.5	13.5
Patients, group 2	12	14.7	14.6	14.5	14.1	14.1
Control subjects	21	13.1	12.4	14.5	12.4	11.7

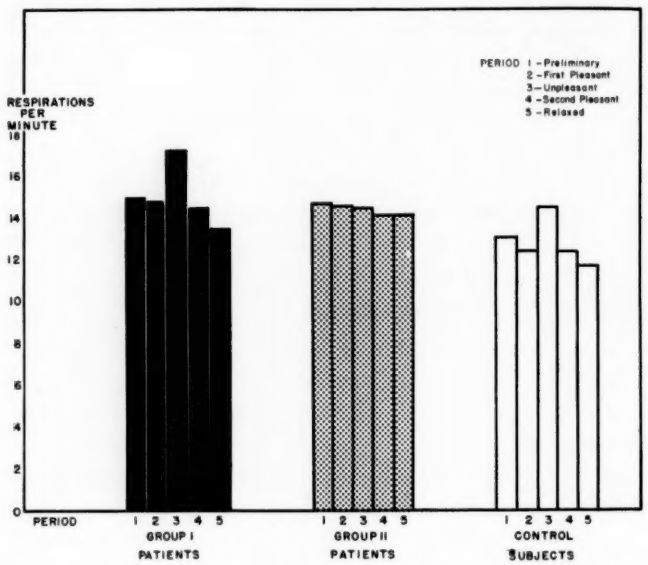

Fig. 13.—Chart showing mean rate of respiration during each period for patients of group 1, for patients of group 2 and for the control subjects.

The individuals of each group did not all show the changes in respiratory rate that are indicated by these group mean values. A few of the patients of group 1, for example, showed little or no difference in rate between the pleasant periods and the unpleasant period. Table 4 was, therefore, arranged to show the proportion of subjects with changes from period to period that conformed to the group mean changes given in table 3, and also to show the proportion that behaved differently. The table thus provides an index of the consistency of the changes. In this summary table each period is compared separately with each of the four other periods so that, in all, comparative data are presented for ten pairs of periods (column 1). For each pair of periods the data are presented first for all the patients, then separately for group 1, for group 2 and, finally, for the

controls (column 2). The number of patients involved in each comparison is shown in column 3. Since the data for one or more of the periods are lacking for some of the patients, the numbers in column 3 are not identical with the number of subjects in each group. Section 1 (columns 4 to 7) deals with the subjects whose rate was greater for the second of the two periods compared. The number of subjects showing this change is given in column 4 and is converted into percentages of the group in column 5. The mean increase in respiratory rate for these subjects in this comparison is shown in column 6, and the range of the differences from which this mean was derived, in column 7. In section 2 (columns 8 to 11) the data are similarly tabulated for subjects whose rate was slower for the second of the two periods compared. Section 3 refers to the subjects whose rate of respiration was equal for the two periods; column 12 gives their number, and column 13, the percentages of the group. Similar tables (tables 7, 10, 13 and 16) summarize the data for depth of respiration, minute respiratory volume, metabolic rate and expiratory-inspiratory angle.

Comparison of Pleasant Periods with the Preliminary Period and with Each Other.—The mean respiratory rate for the pleasant periods for each group was slightly lower than the rate for the preliminary period (table 3). However, this difference did not represent a consistent change shown by most of the subjects of each group. A decrease in rate from the preliminary to the first pleasant period was shown by less than half the patients of group 1 and 2 and by 58 per cent of the controls. Similarly, the rate for the second pleasant period was less than that for the preliminary period in about half the patients in groups 1 and 2 and in less than half the controls. There was little difference between the rates for the two pleasant periods. One fourth of the patients of group 1 and of the controls and over one half of the patients of group 2 had the same rate for the two periods.

Comparison of the Unpleasant Period with the Preliminary Period, the Two Pleasant Periods and the Relaxed Period.—Patients in group 1 and the control subjects had a greater mean respiratory rate during the unpleasant period than during the preliminary period. This change was shown by 65 per cent of group 1 (a mean increase in rate of 3.6 respirations per minute[21]) and by 70 per cent of the controls (a mean increase in rate of 2.5 respirations per minute). For these two groups the mean rate for the unpleasant period was also greater than the rate for the two pleasant periods. This change was shown by 70 per cent of patients in group 1 and by 83 per cent of the controls in the comparison of the first pleasant and the unpleasant period (the mean increases for the subjects of the two groups being, respectively, 4.3 and 3 respirations per minute); it appeared for 82 per cent of patients in group 1 and for 56 per cent of the controls in the comparison of the unpleasant and the second pleasant period (the mean decrease was 2.9 respirations per minute for the patients of group 1 and 3 respirations per minute for the controls). An acceleration for group 2 during the unpleasant period is not evident from table 3, and from table 4 it appears that less than half this group had an accelerated rate during the unpleasant period.

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21. The mean increase in rate shown by 17 of the patients in group 1, which is to be found in table 4, column 6, in the comparison of the preliminary and the unpleasant period, must be distinguished from the difference between the mean rate for all the patients of group 1 during these two periods. This difference, as calculated from the mean rates in table 3, is 2.3 respirations per minute.

TABLE 4.—*Summary of Changes in Rate of Respiration Per Minute on Comparison of Various Periods*

Comparison of Two Periods	Groups of Subjects	No. in Group	1 Subjects Showing Increase During Second Period				2 Subjects Showing Decrease During Second Period				3 Subjects Showing No Change	
			No. of Subjects	Percentage of Group	Increase in Rate per Minute		No. of Subjects	Percentage of Group	Decrease in Rate per Minute		No. of Subjects	Percentage of Group
					Mean	Range			Mean	Range		
A Preliminary and first pleasant period	Total number of patients	35	15	43	1.8	1-3	15	43	2.8	1-7	5	14
	Group 1	24	11	46	1.9	1-3	10	42	3.0	1-6	3	12
	Group 2	11	4	36	1.8	1-2	5	46	2.4	1-6	2	18
	Controls	19	2	10	1.0	1-1	11	58	1.5	1-2	6	32
B First pleasant and unpleasant period	Total number of patients	38	24	63	3.8	1-12	5	13	3.2	2-4	9	24
	Group 1	27	19	70	4.3	1-12	3	11	3.0	2-4	5	19
	Group 2	11	5	46	2.0	1-3	2	18	3.5	3-4	4	36
	Controls	18	15	83	3.0	1-6	1	6	1.0		2	11
C Unpleasant and second pleasant period	Total number of patients	34	4	12	2.5	1-3	25	73	2.7	1-12	5	15
	Group 1	22	0	0	0	0	18	82	2.9	1-12	4	18
	Group 2	12	4	33	2.5	1-3	7	58	2.0	1-5	1	9
	Controls	16	2	13	1.5	1-2	9	56	3.0	1-6	5	31
D Second pleasant and relaxed period	Total number of patients	26	9	35	1.3	1-2	10	38	2.1	1-5	7	27
	Group 1	15	6	40	1.1	1-2	6	40	2.3	1-5	3	20
	Group 2	11	3	28	1.7	1-2	4	36	1.7	1-3	4	36
	Controls	14	2	14	1.5	1-2	9	64	1.9	1-5	3	22
E Preliminary and unpleasant period	Total number of patients	38	21	55	3.7	1-8	11	29	1.6	1-4	6	16
	Group 1	26	17	65	3.6	1-8	6	23	1.3	1-2	3	12
	Group 2	12	4	34	3.0	1-5	5	33	2.0	1-4	3	33
	Controls	20	14	70	2.5	1-6	2	10	2.5	2-3	4	20
F Preliminary and second pleasant period	Total number of patients	31	11	34	2.4	1-5	16	50	2.4	1-5	4	16
	Group 1	19	6	31	3.2	1-5	10	53	2.4	1-4	3	16
	Group 2	12	5	42	1.4	1-2	6	50	2.3	1-5	1	8
	Controls	16	6	37	2.0	1-6	7	44	1.6	1-3	3	19
G Preliminary and relaxed period	Total number of patients	24	7	29	3.0	1-6	16	67	2.8	1-6	1	4
	Group 1	13	4	31	3.0	1-6	9	69	3.2	1-5	0	0
	Group 2	11	3	27	2.7	1-4	7	64	2.6	1-6	1	9
	Controls	15	1	7	5.0		10	66	1.8	1-4	4	27
H First pleasant and second pleasant period	Total number of patients	31	9	30	1.8	1-3	11	35	2.2	1-5	11	35
	Group 1	20	8	40	1.8	1-3	7	35	2.7	1-5	5	25
	Group 2	11	1	9	2.0		4	36	1.2	1-2	6	55
	Controls	14	7	50	2.0	1-5	3	21	1.3	1-2	4	29
I First pleasant and relaxed period	Total number of patients	26	10	38	1.9	1-4	13	50	2.7	1-6	3	12
	Group 1	15	7	47	2.0	1-4	7	47	3.6	1-6	1	6
	Group 2	11	3	27	1.6	1-2	6	55	1.6	1-2	2	18
	Controls	15	5	33	2.0	1-4	7	47	1.7	1-3	3	20
J Unpleasant and relaxed period.	Total number of patients	26	2	8	3.5	3-4	20	77	3.3	1-11	4	15
	Group 1	15	0	0	0	0	13	87	3.8	1-11	2	13
	Group 2	11	2	18	3.5	3-4	7	64	2.1	1-6	2	18
	Controls	15	0	0	0	0	14	93	3.0	1-7	1	7

The greatest difference in mean rate for group 1 and for the controls involved the comparison of the unpleasant and the relaxed period; about 90 per cent of these two groups breathed considerably more slowly during the relaxed than during the unpleasant period (mean decrease in rate, 3.8 respirations per minute for the patients of groups 1 and 3 respirations per minute for the controls). A slight change in the same direction was shown for these two periods by the patients of group 2; about two thirds of the persons in this group showed a mean decrease of 2.1 respirations per minute for the relaxed period as compared with the unpleasant period.

Comparison of Relaxed Period with the Preliminary and the Two Pleasant Periods.—The mean rate of respiration for the relaxed period was lower for each group than the rates for all the other periods. This slowing actually appeared for only two thirds of the subjects in each group in the comparison of the preliminary and the relaxed period, for only one half of the subjects of each group in the comparison of the first pleasant and the relaxed period and for scarcely more than one third of all the patients in the comparison of the second pleasant and the relaxed period. In the last comparison about two thirds of the controls showed a change in this direction, namely, slower respirations for the relaxed than for the second pleasant period.

Summary.—The most striking and consistent change in respiratory rate was the acceleration for the unpleasant period as compared with the other periods, especially with the relaxed period, for the patients of group 1 and for the controls. The acceleration was more pronounced for group 1 and did not occur for group 2. There was a close similarity in rate for the first and the second pleasant period.

DEPTH OF RESPIRATION

The values for the depth of respiration for the 41 patients and 21 control subjects during the five periods are given in table 5. The values given for each subject represent mean values for each period. They ranged from 230 to 1,010 cc. for the patients of group 1, from 220 to 830 cc. for the patients of group 2 and from 210 to 840 cc. for the controls. Mean values derived for all the patients, as well as for groups 1 and 2 separately and for the controls, for each period are given in table 6.

The mean depth of respiration for patients in group 1 varied from 423 cc., for the first pleasant period, to 653 cc., for the unpleasant period, which is a difference of 230 cc. For patients in group 2 the mean depth varied by only 31 cc.—from 405 cc., for the first pleasant period, to 436 cc., for the relaxed period. For the controls the depth, again, was least for the first pleasant period, being 417 cc., and the largest value, 473 cc., occurred during the relaxed period; the difference between the two was 56 cc. For each group the values for the two pleasant periods were similar, the greatest difference between the two periods being 23 cc. for the controls. For group 1 and for the controls the mean depth for the unpleasant period exceeded that for the two pleasant periods. The difference amounted to over 200 cc. for group 1, and to less than 40 cc. for the controls.

TABLE 5.—*Average Depth of Inspiration, Expressed in Cubic Centimeters, for Each Period*

No.	Preliminary Period		First Pleasant Period		Unpleasant Period		Second Pleasant Period		Relaxed Period	
	Duration of Period, Min.	Average Depth per Min., Cc.	Duration of Period, Min.	Average Depth per Min., Cc.	Duration of Period, Min.	Average Depth per Min., Cc.	Duration of Period, Min.	Average Depth per Min., Cc.	Duration of Period Min.	Average Depth per Miin., Cc.
					Patients					
1	7	340	6	340	6	390	..	...	..	...
2	..	...	9	490	6	830	5	320	..	...
3	6	500	7	350	5	520	6	310	8	420
4	..	...	7	310	7	380	8	280	5	360
5	6	780	6	880	6	440	6	780	6	940
6	..	...	6	280	6	340	6	280	6	280
7	6	430	8	380	7	620	6	630	6	500
8	3	860	6	960	7	1,010	7	740	7	290
9	6	390	6	360	7	650	10	400	2	560
10	3	320	3	340	3	420	3	240	3	340
11	3	400	3	440	3	700	3	420	3	380
12	3	440	3	440	3	940	3	380	..	...
13	3	270	3	280	3	350	3	300	3	240
14	3	360	3	400	3	490	3	450	3	460
15	3	730	3	550	3	700	3	820	3	570
16	6	410	7	350	6	400	6	330	6	290
17	3	310	3	370	3	330	3	230	..	...
18	3	410	3	350	3	620	..	...	..	...
19	3	340	3	330	3	460	..	...	..	...
20	6	370	3	310	3	350	3	300	..	...
21	3	620	3	750	3	700	..	...	..	...
22	3	410	3	390	3	500	3	350	3	330
23	3	640	3	390	3	930	..	...	..	...
24	3	330	3	300	3	330	3	310	3	310
25	3	540	3	390	3	460	3	870	3	660
26	3	310	3	290	3	250	..	...	..	...
27	3	410	..	...	3	370	3	370	..	...
28	3	500	..	...	3	500	3	500	..	...
29	3	500	3	380	3	340	..	...	..	...
30	6	400	7	380	3	320	3	380	3	420
31	3	260	..	...	3	220	3	240	..	...
32	6	520	6	500	6	420	7	480	6	380
33	6	420	6	380	6	400	6	360	6	360
34	6	380	8	320	6	370	6	370	6	340
35	6	400	8	440	6	430	7	410	6	450
36	6	290	6	270	7	340	5	300	6	290
37	6	340	6	330	6	340	7	350	6	360
38	6	490	6	410	6	500	6	410	6	380
39	6	410	7	330	7	410	6	320	2	310
40	6	680	6	520	9	610	6	780	6	830
41	3	530	3	570	3	530	3	530	3	680
					Control Subjects					
1	6	720	6	520	6	660	7	600	7	670
2	3	400	3	380	4	400	4	400	4	420
3	6	470	6	420	6	350	6	310	3	350
4	6	380	6	420	5	410	2	390	9	460
5	6	460	7	480	6	420	6	500	6	580
6	6	360	6	400	6	300	6	330	6	320
7	6	400	12	430	6	400	..	...	7	440
8	3	410	3	460	3	490	3	480	3	420
9	3	460	3	440	3	540	3	360	3	660
10	6	680	6	660	6	800	6	660	6	840
11	3	330	3	250	3	370	..	...	..	...
12	3	210	..	...	3	520	3	370	..	...
13	3	330	3	350	3	410	3	330	3	330
14	3	340	3	340	3	340	3	320	3	360
15	3	410	..	...	3	500	3	410	..	...
16	3	390	3	340	3	390	..	...	..	...
17	3	540	3	440	3	480	..	...	..	...
18	3	360	3	360	..	...	..	...	..	...
19	3	440	3	390	3	370	3	440	3	420
20	3	560	3	460	3	580	3	480	3	440
21	3	400	3	360	3	360	3	360	3	380

Table 7 summarizes the differences in depth of respiration for the five periods for each group of subjects. The table is arranged like table 4, and presents the data in terms of ten comparisons of two periods.

Comparison of Two Pleasant Periods with the Preliminary Period and with Each Other.—A little over one-half the patients of group 1 and of the controls showed shallower breathing during the two pleasant periods than during the preliminary period. The mean change was about 80 cc. for the patients in group 1 and about 70 cc. for the controls. The proportion of patients in group 2 showing a similar, though slightly smaller, change (about 50 cc.) was over 80 per cent for the first pleasant period and less than 60 per cent for the second pleasant period.

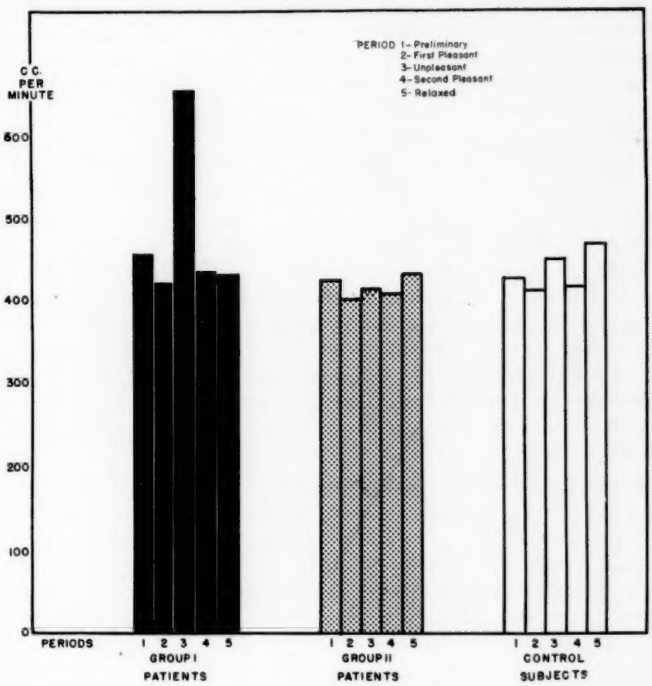

Fig. 14.—Chart showing mean depth of respiration during each period for patients of group 1, for patients of group 2 and for the control subjects.

TABLE 6.—*Mean Depth of Respiration Per Minute During Each Period*

Group	Number	Preliminary Period	First Pleasant Period	Unpleasant Period	Second Pleasant Period	Relaxed Period
All patients	41	442	428	548	426	448
Patients, group 1	29	458	423	653	437	434
Patients, group 2	12	427	405	416	411	436
Controls	21	432	417	455	422	473

There was little difference between the mean depth of respiration for the two pleasant periods; for each group the value was slightly greater for the second pleasant period. It can be seen from table 7 that the number of subjects whose depth of respiration decreased during the second as compared with the first pleasant period was greater than the number whose depth of breathing was increased for the second as compared with the first pleasant period. Yet the mean depth for each group appeared slightly greater for the second pleasant period, owing to the larger individual changes shown by the smaller group of subjects who breathed more deeply during the second pleasant period.

Comparison of Unpleasant Period with the Preliminary Period, with the Two Pleasant Periods and with the Relaxed Period.—For the patients taken as a whole and for the patients in group 1 the mean depth of respiration was greatest during the unpleasant period. The proportion of patients in group 1 who breathed more deeply during the unpleasant period than during the other periods was 62 per cent for the preliminary period, 81 per cent for the first pleasant period, 73 per cent for the second pleasant period and 88 per cent for the relaxed period. The mean difference in depth for these comparisons ranged from 150 to 180 cc. For the controls the mean depth for the unpleasant period was greater than for the preliminary and pleasant periods. The consistency of the changes, as indicated by the proportion of the controls who conformed, was not high. For the three comparisons this proportion varied from about one half to two thirds of the group. The mean excess in depth for the unpleasant period ranged from 82 to 113 cc. About three fourths of the control group breathed somewhat more deeply in the relaxed than in the unpleasant period, and the mean depth for the relaxed period slightly exceeded that for the unpleasant period for this group. In group 2 the depth of breathing was less for the unpleasant period than for the preliminary and relaxed periods, and there was little difference between the unpleasant period and the pleasant periods. The individual changes involved were small and showed no consistency.

Comparison of Relaxed Period with the Preliminary and with the Two Pleasant Periods.—The patients in group 1 showed no pronounced or consistent change in depth of breathing for the relaxed period as compared with the preliminary and the pleasant periods. About two thirds of the patients in group 2 breathed more deeply in the relaxed than in the first pleasant period, and the mean depth for the relaxed period exceeded that for the first pleasant period by about 30 cc. Otherwise the patients in this group showed no greater changes for these comparisons than did those in group 1. For the controls the depth of breathing was maximum during the relaxed period, the mean difference between this period and the preliminary and pleasant periods amounting to about 50 cc. The consistency of this increase in depth for the relaxed period was not great; for the three comparisons the proportion of patients who showed this change ranged from one-half to three-fourths.

Summary.—The only striking changes in the mean value for the depth of respiration were those in group 1 for comparisons B (first pleasant and unpleasant periods), C (unpleasant and second pleasant periods) and E (preliminary and unpleasant periods). In each of these comparisons most of the patients in group 1 showed deeper breathing during the unpleasant period. In these comparisons less striking changes in the same direction were shown by the controls. The mean changes

TABLE 7.—*Summary of Changes in Average Depth of Respiration Per Minute on Comparison of Various Periods*

Comparison of Two Periods	Groups of Subjects	No. in Group	1 Subjects Showing Increase During Second Period				2 Subjects Showing Decrease During Second Period				3 Subjects Showing No Change	
			No. of Subjects	Percentage of Group	Increase in Average Depth per Min., Cc. Mean	Increase in Average Depth per Min., Cc. Range	No. of Subjects	Percentage of Group	Decrease in Average Depth per Min., Cc. Mean	Decrease in Average Depth per Min., Cc. Range	No. of Subjects	Percentage of Group
A Preliminary and first pleasant period	Total number of patients	35	10	28	58	10-130	23	66	73	10-250	2	6
	Group 1	24	8	33	68	10-130	14	59	85	10-250	2	8
	Group 2	11	2	18	40	40- 40	9	82	54	10-160	0	0
	Controls	19	6	32	33	20- 50	11	58	66	20-200	2	11
B First pleasant and unpleasant period	Total number of patients	37	28	76	145	10-540	9	24	89	10-440	0	0
	Group 1	26	21	81	174	30-540	5	19	122	40-440	0	0
	Group 2	11	7	64	58	10- 90	4	36	47	10- 80	0	0
	Controls	18	10	56	82	20-140	6	33	48	10-100	2	11
C Unpleasant and second pleasant period	Total number of patients	34	9	27	147	1-410	21	61	142	10-560	4	12
	Group 1	22	4	18	220	10-410	16	73	181	20-560	2	9
	Group 2	12	5	42	80	20-170	5	42	40	10- 90	2	16
	Controls	16	3	19	60	30- 80	11	69	113	10-400	2	12
D Second pleasant and relaxed period	Total number of patients	27	11	41	106	20-180	13	48	83	10-450	3	11
	Group 1	16	6	38	103	10-160	8	50	150	20-450	2	12
	Group 2	11	5	45	58	10-150	5	45	36	10-100	1	10
	Controls	14	9	65	91	20-300	4	28	32	10- 60	1	7
E Preliminary and unpleasant period	Total number of patients	38	19	50	96	10-500	14	37	76	10-340	5	13
	Group 1	26	16	62	162	20-500	8	31	92	10-340	2	7
	Group 2	12	3	25	30	10- 50	6	50	53	10-100	3	25
	Controls	20	9	45	94	20-310	7	35	64	40-120	4	20
F Preliminary and second pleasant period	Total number of patients	31	11	36	82	10-330	17	55	66	10-190	3	10
	Group 1	11	7	37	110	10-330	10	53	80	20-190	2	11
	Group 2	12	4	33	33	10-100	7	58	46	10- 90	1	9
	Controls	16	4	25	70	10-160	8	50	71	20-160	4	25
G Preliminary and relaxed period	Total number of patients	25	11	44	94	20-170	13	56	110	20-570	0	0
	Group 1	14	6	43	107	20-170	8	57	135	20-570	0	0
	Group 2	11	5	45	78	20-150	5	45	70	40-110	1	10
	Controls	15	8	53	81	10-200	6	40	61	20-120	1	7
H First pleasant and second pleasant period	Total number of patients	31	11	36	134	10-480	17	55	63	10-220	3	10
	Group 1	20	7	35	160	10-480	12	60	79	10-220	1	5
	Group 2	11	4	36	90	20-260	5	46	24	10- 40	2	18
	Controls	14	6	43	35	20- 80	6	43	55	20-110	2	14
I First pleasant and relaxed period	Total number of patients	27	16	59	88	10-310	9	33	120	20-670	2	8
	Group 1	16	9	57	95	10-210	5	31	178	40-670	2	12
	Group 2	11	7	64	77	10-310	4	36	47	20-120	0	0
	Controls	15	11	74	76	10-220	4	26	40	20- 80	0	0
J Unpleasant and relaxed period.	Total number of patients	27	7	26	174	10-500	20	74	123	20-720	0	0
	Group 1	16	2	12	350	200-500	14	88	148	20-720	0	0
	Group 2	11	5	45	102	20-220	6	55	63	30-120	0	0
	Controls	15	11	74	50	10-160	3	20	76	70-140	1	6

throughout for group 2 were relatively small in either direction. In the other comparisons, whenever an appreciable change in depth of respiration occurred in one direction a comparable change was also observed in the opposite direction. On the whole, the effect of change in ideational content on depth of respiration appeared to be variable and inconsistent.

MINUTE RESPIRATORY VOLUME

The minute respiratory volumes for the 41 patients and 21 controls during the successive periods are shown in table 8. The values varied for group 1 from 3.1 to 14.5 liters, for group 2 from 3.8 to 9.2 liters and for the controls from 3.1 to 9.4 liters. Mean values derived from these individual figures for the patients of group 1, for the patients of group 2 and for the controls are presented in table 9.

The mean values for the minute respiratory volume varied during the five successive periods from 5.3 to 8.4 liters for group 1, from 5.7 to 6.2 liters for group 2 and from 5 to 6.1 liters for the controls. Thus, group 1 showed the largest values for the minute respiratory volume and the greatest range of variation from period to period. The lowest values were those for the control group during the first pleasant and the relaxed period. The changes from period to period for this group, while not quite so pronounced as those for group 1, were nevertheless similar. For both groups, the minute respiratory volume rose sharply to a maximum during the unpleasant period and returned during the second pleasant period to the same value as that for the first pleasant period.

Table 10 summarizes the differences in mean minute respiratory volume for the five periods for each group of subjects. It is arranged like table 4 and 7, and presents the data in terms of ten comparisons of two periods.

Comparison of Two Pleasant Periods with the Preliminary Period and with Each Other.—For each group of subjects the minute respiratory volume was less for the two pleasant periods than for the preliminary period. The change was fairly consistent for the comparison of the preliminary and the first pleasant period, the proportion of subjects reacting in this way being about 80 per cent for group 1 and the controls and 73 per cent for group 2. The proportion showing a decrease in minute respiratory volume in the second pleasant period as compared with the preliminary period was only slightly more than one-half for group 1 and about two-thirds for group 2 and the control group. The mean decrease in ventilation shown by these subjects was 1.5 and 2 liters for group 1 and less than 1 liter for group 2 and the controls. For each group the mean minute respiratory volume for the second pleasant period was the same as that for the first pleasant period, and in each case there was about an even division of the subjects who had a slight increase and those who had a slight decrease in ventilation for the second as compared with the first pleasant period.

Comparison of Unpleasant Period with the Preliminary Period, with the Two Pleasant Periods and with the Relaxed Period.—For group 1 and for the controls the minute respiratory volume was consistently higher during the unpleasant period than during the four other periods. For group 1 the consistency of this increase ranged from 86 per cent, for the comparison of the unpleasant and the second pleasant period, to 100 per cent, for the comparison of the unpleasant and

TABLE 8.—*Average Minute Respiratory Volume, Expressed in Liters, for Each Period*

No.	Preliminary Period		First Pleasant Period		Unpleasant Period		Second Pleasant Period		Relaxed Period	
	Duration of Period, Min.	Average Minute Volume, Liters	Duration of Period, Min.	Average Minute Volume, Liters	Duration of Period, Min.	Average Minute Volume, Liters	Duration of Period, Min.	Average Minute Volume, Liters	Duration of Period, Min.	Average Minute Volume, Liters
					Patients					
1	7	4.6	6	4.8	6	6.4	..	...	..	...
2	..	...	9	7.0	6	12.7	5	6.0	..	...
3	6	11.0	7	8.4	5	12.6	6	7.2	8	7.7
4	..	...	7	4.4	7	9.0	8	3.8	5	4.6
5	6	8.7	6	4.5	6	7.4	6	4.2	6	7.0
6	..	...	6	4.8	6	6.2	6	4.3	6	4.2
7	6	5.0	8	4.5	7	6.4	6	4.8	6	4.0
8	3	13.2	6	8.1	7	14.2	7	8.0	7	6.3
9	6	5.5	6	5.5	7	7.5	10	4.5	2	5.4
10	3	4.4	3	3.9	3	8.3	3	3.1	3	3.9
11	3	3.4	3	4.3	3	7.6	3	3.6	3	4.6
12	3	4.7	3	4.5	3	11.2	3	3.4	..	...
13	3	5.8	3	5.6	3	8.7	3	6.5	3	5.7
14	3	4.3	3	3.5	3	5.4	3	4.3	3	4.1
15	3	5.1	3	4.8	3	6.1	3	5.8	3	4.8
16	6	8.7	7	7.8	6	10.0	6	7.3	6	5.5
17	3	9.3	3	7.9	3	12.1	3	8.1	..	...
18	3	8.8	3	5.7	3	12.4	..	...	..	...
19	3	5.3	3	4.7	3	6.3	..	...	..	...
20	6	5.3	3	4.7	3	7.1	3	5.9	..	...
21	3	5.2	3	4.5	3	6.3	..	...	..	...
22	3	7.2	3	7.8	3	11.3	3	8.4	3	7.5
23	3	10.3	3	7.2	3	14.5	..	...	..	...
24	3	4.0	3	4.0	3	5.1	3	4.9	4	4.7
25	3	4.8	3	4.2	3	5.2	3	5.3	3	4.5
26	3	4.6	3	4.3	3	5.2	..	...	..	...
27	3	5.1	..	...	3	5.6	3	5.7	..	...
28	3	6.2	..	...	3	6.0	3	6.0	..	...
29	3	8.3	3	6.3	3	5.8	..	...	..	...
30	6	5.7	3	4.4	3	4.9	3	3.9	3	4.1
31	3	4.9	..	...	3	4.5	3	4.5	..	...
32	6	6.0	6	6.6	6	6.7	7	6.6	6	6.8
33	6	7.7	6	7.4	6	7.8	6	7.2	6	7.1
34	6	8.2	8	5.5	6	6.8	6	6.4	6	6.7
35	6	3.8	8	3.9	6	4.0	7	3.9	6	4.2
36	6	5.5	6	5.1	7	6.2	5	5.4	6	5.3
37	6	5.1	6	5.0	6	5.1	7	5.0	6	5.1
38	6	6.6	6	6.5	6	6.4	6	6.6	6	6.6
39	6	8.2	7	6.3	7	7.9	6	6.6	2	5.5
40	6	7.5	6	6.9	9	8.1	6	9.2	6	9.0
41	3	4.6	3	4.5	3	4.8	3	4.3	3	4.3
					Control Subjects					
1	6	9.4	6	5.5	6	7.5	7	6.6	7	7.0
2	3	5.1	3	4.8	4	5.2	4	5.1	4	5.0
3	6	7.1	6	6.8	6	7.6	6	6.5	3	7.2
4	6	5.5	6	5.9	5	5.0	2	6.0	9	5.6
5	6	5.4	7	4.6	6	6.1	6	4.5	6	4.6
6	6	4.5	6	4.5	6	5.5	6	4.4	6	3.9
7	6	5.5	12	5.4	6	6.7	..	...	7	5.5
8	3	5.8	3	5.6	3	6.9	3	6.9	3	5.8
9	3	5.4	3	4.8	3	7.8	3	4.5	3	5.3
10	6	4.9	6	4.9	6	6.1	6	4.0	6	4.1
11	3	5.5	3	4.9	3	5.9	..	...	..	...
12	3	5.7	..	...	3	6.0	3	5.1	..	...
13	3	4.8	3	4.6	3	6.4	3	4.4	3	4.6
14	3	4.4	3	4.1	3	4.7	3	4.2	3	3.9
15	3	3.6	..	...	3	4.6	3	3.8	..	...
16	3	5.8	3	5.3	3	6.2	..	...	..	...
17	3	6.7	3	5.8	3	7.8	..	...	..	...
18	3	5.4	3	4.7	..	...	..	...	..	...
19	3	6.1	3	5.7	3	6.2	3	5.3	3	5.2
20	3	4.4	3	3.1	3	5.1	3	3.3	3	3.3
21	3	4.8	3	4.7	3	5.4	3	5.0	3	4.5

the relaxed period. For the controls the consistency ranged from 86 per cent, for the comparison of the unpleasant and the second pleasant period, to 95 per cent, for the comparison of the unpleasant and the first pleasant period. For each of the four comparisons the mean increase in ventilation was about two and

TABLE 9.—*Mean Values for Minute Respiratory Volume, Expressed in Liters*

Group	Number	Preliminary Period	First Pleasant Period	Unpleasant Period	Second Pleasant Period	Relaxed Period
All patients	41	6.1	5.5	7.8	5.6	5.5
Patients, group 1	29	6.1	5.5	8.4	5.5	5.3
Patients, group 2	12	6.2	5.7	6.1	5.8	5.9
Controls	21	5.5	5.0	6.1	5.0	5.0

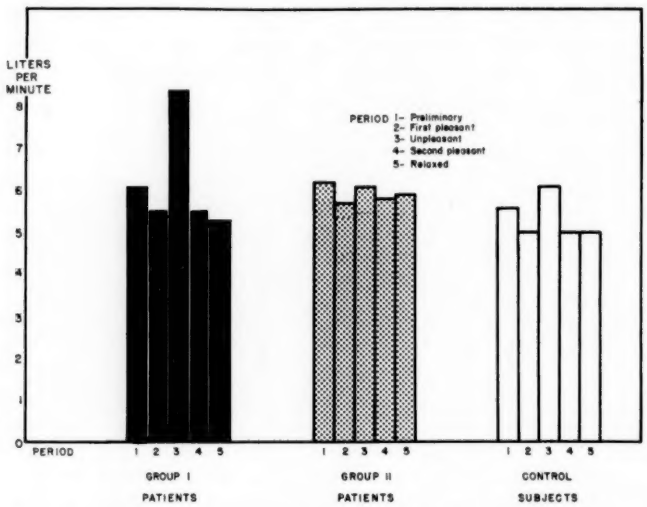

Fig. 15.—Chart showing mean minute respiratory volume during each period for patients of group 1, for patients of group 2 and for the control subjects.

one-half times as great for group 1 as for the controls, ranging from 2.1 to 3.4 liters for the former and from 0.8 to 1.3 liters for the latter. For group 2 the mean minute respiratory volume for the unpleasant period was greater by only 0.4 liter than the mean value for the first pleasant period and by only 0.3 liter than the mean value for the second pleasant period. The consistency of these small differences was 91 and 75 per cent, respectively, for the two comparisons. For group 2 the minute respiratory volume for the unpleasant period was not greater than that for the preliminary period. There was a slight excess in mean minute respiratory volume for the unpleasant as compared with the relaxed period for this group, but this change was shown by only 55 per cent of the individual subjects.

Comparison of Relaxed Period with the Preliminary Period and with the Two Pleasant Periods.—For group 1 and for the control group the mean minute respiratory volume was lower for the relaxed than for the preliminary period. The consistency of the change was about the same for the two groups, namely,

TABLE 10.—*Summary of Changes in Minute Respiratory Volume on Comparison of Various Periods*

Comparison of Two Periods	Groups of Subjects	No. in Group	1 Subjects Showing Increase During Second Period				2 Subjects Showing Decrease During Second Period				3 Subjects Showing No Change	
			No. of Subjects	Percentage of Group	Increase in Liters per Minute		No. of Subjects	Percentage of Group	Decrease in Liters per Minute		No. of Subjects	Percentage of Group
					Mean	Range			Mean	Range		
A Preliminary and first pleasant period	Total number of patients	35	6	17	0.7	0.1-1.9	27	77	1.23	0.1-5.1	2	6
	Group 1	24	3	13	0.6	0.2-0.9	19	79	1.46	0.2-5.1	0	8
	Group 2	11	3	27	0.9	0.1-1.9	8	73	0.5	0.1-2.7	0	0
	Controls	19	1	5	0.4		16	84	0.7	0.1-3.9	2	11
B First pleasant and unpleasant period	Total number of patients	38	36	95	2.5	0.1-7.3	2	5	0.3	0.1-0.5	0	0
	Group 1	27	26	96	3.2	0.9-7.3	1	4	0.5		0	0
	Group 2	11	10	95	0.6	0.1-1.6	1	9	0.1		0	0
	Controls	18	17	95	1.3	0.4-3.0	1	5	0.9		0	0
C Unpleasant and second pleasant period	Total number of patients	34	4	12	0.4	0.1-0.2	28	82	2.5	0.1-7.8	2	6
	Group 1	22	2	9	0.1	0.1-0.1	19	86	3.42	0.2-7.8	1	5
	Group 2	12	2	17	0.7	0.2-1.1	19	75	0.5	0.1-1.3	1	8
	Controls	14	1	7	1.0		14	94	1.3	0.1-3.3	1	7
D Second pleasant and relaxed period	Total number of patients	27	11	41	0.7	0.1-2.8	14	52	0.7	0.1-1.8	2	7
	Group 1	16	6	37	1.1	0.5-2.8	10	63	0.8	0.1-1.8	0	0
	Group 2	11	5	46	0.2	0.1-0.3	4	36	0.4	0.1-1.1	2	18
	Controls	14	6	43	0.4	0.1-1.8	7	50	0.4	0.1-1.1	1	7
E Preliminary and unpleasant period	Total number of patients	38	29	76	1.8	0.1-6.5	8	21	0.89	0.2-2.5	1	3
	Group 1	26	23	89	2.1	0.4-6.5	3	11	0.13	0.2-2.5	0	0
	Group 2	12	6	50	0.4	0.1-0.7	5	42	0.6	0.1-1.4	1	8
	Controls	20	18	90	0.8	0.1-2.4	2	10	1.2	0.5-1.9	0	0
F Preliminary and second pleasant period	Total number of patients	31	11	36	0.7	0.1-1.7	18	58	1.5	0.1-5.1	2	6
	Group 1	19	8	42	0.7	0.2-1.2	10	53	2.0	0.1-5.1	1	5
	Group 2	12	3	25	0.8	0.1-1.1	8	67	0.8	0.1-1.8	1	8
	Controls	16	4	25	0.5	0.2-1.1	11	69	0.8	0.1-2.3	1	6
G Preliminary and relaxed period	Total number of patients	25	6	24	0.8	0.3-1.5	17	68	1.4	0.1-6.9	2	8
	Group 1	14	3	21	0.7	0.3-1.2	11	79	1.7	0.1-6.9	0	0
	Group 2	11	3	27	0.9	0.4-1.5	10	55	1.1	0.1-2.7	2	18
	Controls	15	2	13	0.1	0.1-0.1	11	74	0.7	0.1-1.4	2	13
H First pleasant and second pleasant period	Total number of patients	31	14	45	0.8	0.1-2.3	14	45	0.6	0.1-1.2	3	10
	Group 1	20	9	45	0.8	0.1-1.2	11	55	0.7	0.1-1.2	0	0
	Group 2	11	5	46	0.8	0.1-2.3	3	27	0.3	0.1-0.5	3	27
	Controls	14	7	50	0.5	0.1-1.3	7	50	0.3	0.1-0.9	0	0
I First pleasant and relaxed period	Total number of patients	27	14	52	0.6	0.1-2.5	11	41	0.7	0.1-2.3	2	7
	Group 1	16	7	44	0.7	0.1-2.5	7	44	0.9	0.1-2.3	2	12
	Group 2	11	7	64	0.6	0.1-2.1	4	36	0.4	0.1-8.0	0	0
	Controls	15	7	47	0.4	0.1-1.5	6	40	0.4	0.1-0.8	2	13
J Unpleasant and relaxed period.	Total number of patients	27	4	15	0.4	0.4-1.4	22	81	2.3	0.1-7.9	1	4
	Group 1	16	0	..	...	.....	16	100	2.9	0.4-7.9	0	0
	Group 2	11	4	36	0.3	0.1-0.9	6	55	0.9	0.1-2.4	1	9
	Controls	15	1	7	0.6		14	93	1.2	0.2-2.5	0	0

79 and 74 per cent. The difference in minute respiratory volume involved was again greater for group 1, being 1.7 liters for this group and 0.7 liter for the controls. For both groups the mean minute respiratory volume for the relaxed period was like that for the pleasant periods. In the comparison of the relaxed and the second pleasant period for the patients in group 1, the proportion having a higher minute respiratory volume for the relaxed period (37 per cent) was not equal to that showing the opposite change (63 per cent); since the individual changes involved were small, however, the mean minute respiratory volume for the group was only 0.2 liter less for the relaxed than for the second pleasant period. For group 2 the minute respiratory volume for the relaxed period was like that for the pleasant periods and was only 0.3 liter less than that for the preliminary period.

Summary.—The most outstanding facts to be noted in table 9 are the (1) reversible changes to a greater minute respiratory volume during the unpleasant period than during the pleasant periods for patients in group 1 and for the controls, and (2) the absence of significant changes for the patients in group 2. The changes observed for patients in group 1 and for the controls are more outstanding than the similar changes in the component factors, namely, rate and depth of respiration (tables 3 and 6). Great consistency (about 90 per cent) was observed for the subjects of group 1 and the controls in comparisons B (first pleasant and unpleasant periods), C (unpleasant and second pleasant periods), E (preliminary and unpleasant periods) and J (unpleasant and relaxed periods). In comparison B (first pleasant and unpleasant period) a similar excess minute respiratory volume for the unpleasant period appeared for 95 per cent of patients in group 2, but the mean change was approximately one-fifth that for group 1 and one-half that for the control group.

METABOLIC RATE

Metabolic rates were derived for the five periods from all the respiratory tracings available, even when the period lasted only two or three minutes instead of six minutes, the routine interval for measurements of basal metabolism. In table 11, in which these metabolic rates are presented, the rates that are based on tracings of less than six minutes' duration are marked with an asterisk, and these values must be considered as less reliable than those for the longer period. The individual metabolic rates varied for the patients of group 1 from +44 to −25 per cent, for the patients of group 2 from +20 to −21 per cent and for the controls from +37 to −22 per cent. The mean values for each group for the five periods are shown in table 12.

The mean value for the metabolic rate for patients in group 1 showed a maximum of +1 per cent for the unpleasant period, with relatively lower values for the two pleasant periods and for the relaxed period. For the control group, there was little difference between the mean values for the first four periods,

TABLE 11.—*Metabolic Rate During Various Periods*

No.	Preliminary Period		First Pleasant Period		Unpleasant Period		Second Pleasant Period		Relaxed Period	
	Duration of Period, Min.	Metabolic Rate, %	Duration of Period, Min.	Metabolic Rate, %	Duration of Period, Min.	Metabolic Rate, %	Duration of Period, Min.	Metabolic Rate, %	Duration of Period, Min.	Metabolic Rate, %
					Patients					
1	7	−12	6	− 7	6	− 7	..	....	..	....
2	..	....	9	+ 2	6	+ 7	5	+ 5*	..	....
3	6	− 5	7	−13	5	−10*	6	−10	8	+ 3
4	..	....	7	− 4	7	− 4	8	− 4	5	− 4*
5	6	− 1	6	− 4	6	− 5	6	−11	6	− 1
6	..	....	6	−16	6	−16	6	−11	6	−25
7	6	− 3	8	− 5	7	+ 6	6	− 2	6	+ 6
8	3	+ 1*	6	− 5	7	+14	7	− 3	7	− 4
9	6	− 5	6	− 5	7	− 8	10	+ 4	2	+ 1*
10	3	−14*	3	−25*	3	+20*	3	−17*	3	−24*
11	3	+ 7*	3	+14*	3	+23*	3	+ 4*	3	+17*
12	3	− 6*	3	0*	3	+12*	3	−12*	..	....
13	3	− 1*	3	+ 6*	3	+ 9*	3	− 7*	3	− 1*
14	3	+ 2*	3	− 4*	3	+ 9*	3	− 7*	3	−10*
15	3	−23*	3	−11*	3	− 9*	3	− 7*	3	−23*
16	6	+ 7	7	+ 6	6	+ 1	6	−10	6	− 1
17	3	+25*	3	+25*	3	+44*	3	+22*	..	....
18	3	− 5*	3	−12*	3	+ 6*	..	....	..	....
19	3	− 5*	3	−10*	3	− 5*	..	....	..	....
20	6	−11	3	− 2*	3	−11*	3	−11*	..	....
21	3	−13*	3	−13*	3	− 7*	..	....	..	....
22	3	− 2	3	−23*	3	−23*	3	−15*	3	− 8*
23	3	− 5*	3	−32*	3	− 6*	..	....	..	....
24	3	+ 6*	3	+12*	3	− 7*	3	− 4*	3	− 4*
25	3	−14*	3	−20*	3	− 9*	3	− 9*	3	−20*
26	3	− 8*	3	−11*	3	− 5*	..	....	..	....
27	3	+ 3*	..	....	3	+ 5*	3	+ 3*	..	....
28	3	+33*	..	....	3	+15*	3	− 5*	..	....
29	3	−13*	3	−19*	3	−10*	..	....	..	....
30	6	0	3	−13*	3	−13*	3	−13*	3	−13*
31	3	+ 9*	..	....	3	+ 2*	3	+ 9*	..	....
32	6	+14	6	+ 6	6	− 5	7	− 7	6	−21
33	6	+20	6	+ 1	6	− 7	6	− 8	6	+ 1
34	6	+ 4	8	− 9	6	− 3	6	− 9	6	− 9
35	6	+10	8	+ 4	6	0	7	+ 4	6	+10
36	6	−11	6	−14	7	− 1	5	− 5	6	−14
37	6	−11	6	−14	6	− 1	7	−12	6	−12
38	6	−16	6	− 9	6	− 4	6	− 6	6	−10
39	6	− 8	7	+ 3	7	+ 2	6	0	2	+ 3*
40	6	−11	6	−14	9	−16	6	+ 1	6	−16
41	3	− 5*	3	−14*	3	−10*	3	− 5*	3	0*
					Control Subjects					
1	6	− 5	6	− 9	6	− 1	7	+ 2	7	−12
2	3	+ 1*	3	− 2*	4	− 8*	4	− 6*	4	− 8*
3	6	+ 8	6	+17	6	+ 9	6	+ 8	3	+ 5*
4	6	− 1	6	−11	5	−11*	2	−12*	9	−12
5	6	+34	7	+37	6	+15	6	+15	6	+20
6	6	−16	6	−13	6	− 8	6	−18	6	−19
7	6	−15	12	−13	6	−13	..	....	7	−12
8	3	− 2*	3	+ 3*	3	+ 9*	3	+ 7*	3	−12*
9	3	+10*	3	+10*	3	+ 7*	3	+10*	3	+ 4*
10	6	−20	6	−20	6	− 9	6	−20	6	−20
11	3	−14*	3	−14*	3	−14*	..	....	..	....
12	3	− 3*	..	....	3	+ 6*	3	0*	..	....
13	3	+21*	3	+12*	3	+ 9*	3	+ 2*	3	+ 6*
14	3	−10*	3	−16*	3	−16*	3	−10*	3	−10*
15	3	−16*	..	....	3	+ 3*	3	−11*	..	....
16	3	−11*	3	+ 2*	3	+ 6*	..	....	..	....
17	3	− 1*	3	−10*	3	− 1*	..	....	..	....
18	3	−22*	3	−15*	..	....	..	....	..	....
19	3	− 1*	3	+ 6*	3	+ 1*	3	+ 6*	3	− 4*
20	3	− 1*	3	+ 2*	3	+26*	3	− 1*	3	− 1*
21	3	− 6*	3	− 9*	3	− 9*	3	− 9*	3	− 9*

* The asterisk indicates periods of less than six minutes.

although the highest metabolic rate occurred during the unpleasant period. The lowest mean value for this group was that for the relaxed period. The changes in the mean metabolic rate for group 2 did not show any correlation with the ideas associated with the different periods. The value was highest for the preliminary period and lowest for the first pleasant and the relaxed period, with no appreciable rise for the unpleasant period.

TABLE 12.—*Mean Metabolic Rate During Each Period*

Group	Number	Preliminary Period	First Pleasant Period	Unpleasant Period	Second Pleasant Period	Relaxed Period
All patients	41	−2	−6	−1	−4	−6
Patients, group 1	29	−3	−7	+1	−5	−6
Patients, group 2	12	0	−7	−5	−4	−7
Controls	21	−3	−2	0	−2	−6

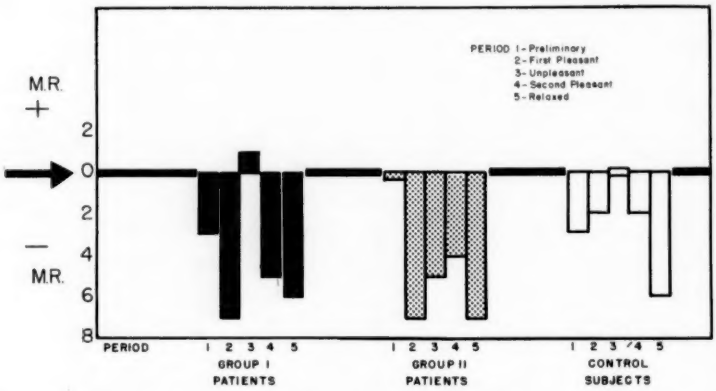

Fig. 16.—Chart showing mean metabolic rates during each period for patients of group 1, for patients of group 2 and for the control subjects.

Table 13 summarizes the individual differences in metabolic rate for the five periods for each group of subjects and is arranged like table 4. For most of the comparisons, the proportion of subjects that showed an increase (column 5) is not very different from the proportion of subjects that showed a change in the opposite direction (column 9). More than half the patients had a somewhat lower metabolic rate during the two pleasant periods than during the preliminary period. This decrease was not shown by the controls. There was no predominating change in either direction in the comparison of the two pleasant periods. For group 1 there was a slight tendency toward an increased metabolic rate during the unpleasant period as compared with the preliminary period, with the two pleasant periods and with the relaxed period. The mean increase for these four comparisons varied from 11.3 to 15.3 per cent, and the proportion of the group showing an increase for each comparison was roughly 60 per cent. The controls also showed a slight tendency toward a higher metabolic rate during the unpleasant period than during the preliminary period, the second pleasant period or the relaxed period. The mean change in this direction was roughly + 10 per cent, and the proportion of the

TABLE 13.—*Summary of Changes in Metabolic Rate on Comparison of Various Periods*

Comparison of Two Periods	Groups of Subjects	No. in Group	1 Subjects Showing Increase During Second Period				2 Subjects Showing Decrease During Second Period				3 Subjects Showing No Change	
			No. of Subjects	Percentage of Group	Increase in Metabolic Rate		No. of Subjects	Percentage of Group	Decrease in Metabolic Rate		No. of Subjects	Percentage of Group
					Mean	Range			Mean	Range		
A Preliminary and first pleasant period	Total number of patients	36	8	22	7.9	5-12	25	70	7.9	1-27	3	8
	Group 1	25	7	28	7.4	5-12	15	60	8.2	1-27	3	12
	Group 2	11	1	9	11.0		10	91	7.6	3-19	0	0
	Controls	19	10	52	6.1	2-13	6	32	6.0	3-10	3	16
B First pleasant and unpleasant period	Total number of patients	38	21	55	12.2	3-45	12	32	5.7	1-19	5	13
	Group 1	27	17	63	12.9	3-45	6	22	6.5	1-19	4	15
	Group 2	11	4	36	9.2	5-13	6	55	5.0	1-11	1	9
	Controls	18	7	39	9.6	4-24	6	33	7.8	3-22	5	28
C Unpleasant and second pleasant period	Total number of patients	34	9	26	7.0	2-17	20	59	11.4	1-37	5	15
	Group 1	22	5	23	6.0	2-12	13	59	15.3	2-37	4	18
	Group 2	12	4	33	8.2	4-17	7	59	4.0	1-11	1	8
	Controls	16	4	25	3.2	2- 5	10	62	8.5	1-27	2	13
D Second pleasant and relaxed period	Total number of patients	27	9	33	8.6	3-13	13	48	8.4	1-17	5	19
	Group 1	16	6	37	10.0	7-13	8	50	7.6	1-16	2	13
	Group 2	11	3	27	6.0	3- 9	5	46	9.8	4-17	3	27
	Controls	14	3	21	4.0	3- 5	6	43	8.7	1-19	5	36
E Preliminary and unpleasant period	Total number of patients	38	19	50	11.1	2-34	17	45	9.8	1-27	2	5
	Group 1	26	15	58	11.3	2-34	9	34	8.2	1-21	2	8
	Group 2	12	4	33	10.5	10-12	8	67	11.3	1-27	0	0
	Controls	20	11	55	10.0	1-27	7	35	8.8	3-19	2	10
F Preliminary and second pleasant period	Total number of patients	31	7	22	7.3	5-16	20	65	10.5	1-38	4	13
	Group 1	19	3	16	10.0	5-16	14	74	9.1	1-38	2	10
	Group 2	12	4	33	9.0	6-12	6	50	13.6	1-28	2	17
	Controls	16	6	38	9.1	3-19	5	31	6.4	3-19	5	31
G Preliminary and relaxed period	Total number of patients	25	7	28	7.8	5-11	14	56	10.4	1-35	4	16
	Group 1	14	4	29	8.2	6-10	7	50	8.1	5-12	3	21
	Group 2	11	3	27	7.3	5-11	7	64	12.7	1-35	1	9
	Controls	15	1	7	7.6		11	73	7.6	3-14	3	20
H First pleasant and second pleasant period	Total number of patients	31	13	42	6.2	2-15	14	46	9.0	3-15	4	13
	Group 1	20	8	40	5.5	2-11	11	55	9.1	3-15	1	5
	Group 2	11	5	46	7.4	2-15	3	27	8.3	3-13	3	27
	Controls	14	4	29	7.7	6-11	6	42	7.3	3-22	4	29
I First pleasant and relaxed period	Total number of patients	27	10	37	5.4	1-16	10	37	12.1	1-27	7	26
	Group 1	16	8	50	5.7	1-16	6	37	9.5	6-16	2	13
	Group 2	11	2	18	4.0	2- 6	4	36	11.0	1-27	5	46
	Controls	15	10	67	6.3	1-12	3	20	7.3	1-17	2	13
J Unpleasant and relaxed period.	Total number of patients	27	8	30	7.8	1-15	15	55	13.0	2-44	4	15
	Group 1	16	5	31	8.8	3-15	9	56	14.7	2-44	2	13
	Group 2	11	3	27	6.3	1-10	6	55	10.3	6-16	2	18
	Controls	15	3	20	4.0	1- 6	10	67	9.7	1-27	2	13

group showing this change was, again, roughly 60 per cent. It thus appears that the metabolic rate rose during the unpleasant period for scarcely more than half of the patients in group 1 and of the controls. There was even less evidence of an increase during the unpleasant period for patients in group 2 than for the other subjects. As a matter of fact, two thirds of patients in group 2 had a lower metabolic rate during the unpleasant period than during the preliminary period. For all the groups there was a tendency toward a lower metabolic rate during the relaxed than during the preliminary period. The consistency varied from 50 per cent, for group 1, to 73 per cent, for the controls. No significant difference in metabolic rate appeared for the relaxed period as compared with the pleasant periods.

Summary.—The present tests showed no marked or consistent correlation between mental content and metabolic rate.

EXPIRATORY-INSPIRATORY ANGLES

The mean expiratory-inspiratory angles [22] calculated from the respiratory tracings of the 41 patients and 21 control subjects during the five successive periods are shown in table 14. For group 1 the mean angle varied from a minimum of 2.4 on the arbitrary scale (patient 23, during the preliminary period) to a maximum of 16.4 (patient 25, during the second pleasant period). For group 2 the minimum was 2.1 (patient 40, second pleasant period), and the maximum was 6.9 (patient 30, second pleasant period). For the controls the minimum was 2.5 (subject 6, unpleasant period), and the maximum was 16.3 (subject 20, second pleasant period). Group mean values for the successive periods derived separately for the patients of group 1, for the patients of group 2 and for the controls are given in table 15.

The range of this average figure was from 4.8, for the unpleasant period, to 6.6, for the second pleasant period, for group 1 and from 5.0, for the unpleasant period, to 7.1, for the relaxed period, for the controls. For group 2 the average mean angle varied from 4.7 to 5.0; in other words, it changed little from period to period.

The group average of the mean expiratory-inspiratory angle during a given period was greatest for the control group during the relaxed period; the corresponding respiratory rate averaged 11.7 per minute, which was the lowest mean rate found for any of the three groups during a given period. In general, when the mean respiratory rates and the corresponding mean expiratory-inspiratory angles were compared for the individual subjects (tables 2 and 14), there appeared to be a tendency for high rates to be associated with low values on the expiratory-inspiratory angle scale (sharp angles) and, vice versa, for low respiratory rates to be associated with broad angles. This relationship can be seen in table 16, in which a selection has been made of the cases in which during one or more

22. From the distribution of the expiratory-inspiratory angles found in the respiratory tracing for each period a mean expiratory-inspiratory angle was calculated for each patient (see section on "Technic"). The mean expiratory-inspiratory angle thus obtained should not be confused with the group mean values, which, in turn, were derived from the individual mean values.

TABLE 14.—*Average Expiratory-Inspiratory Angle*

No.	Preliminary Period		First Pleasant Period		Unpleasant Period		Second Pleasant Period		Relaxed Period	
	Duration of Period, Min.	Average Expiratory-Inspiratory Angle	Duration of Period, Min.	Average Expiratory-Inspiratory Angle	Duration of Period, Min.	Average Expiratory-Inspiratory Angle	Duration of Period, Min.	Average Expiratory-Inspiratory Angle	Duration of Period, Min.	Average Expiratory-Inspiratory Angle
					Patients					
1	7	6.7	6	6.0	6	4.8	..	...	..	...
2	..	...	9	4.2	6	3.8	5	7.2	..	...
3	6	4.2	7	4.4	5	4.1	6	4.6	8	4.1
4	..	...	7	5.6	7	4.6	8	6.6	5	4.5
5	6	5.6	6	12.8	6	3.5	6	12.6	6	6.5
6	..	...	6	5.1	6	5.3	6	7.2	6	6.0
7	6	6.1	8	7.7	7	6.7	6	14.0	6	13.5
8	3	3.4	6	5.1	7	3.6	7	4.0	7	5.2
9	6	3.5	6	3.6	7	4.7	10	4.5	2	5.0
10	3	4.9	3	5.4	3	3.3	3	5.8	3	5.0
11	3	6.1	3	4.4	3	4.3	3	8.2	3	4.5
12	3	6.5	3	5.8	3	4.8	3	7.4	..	...
13	3	4.4	3	3.8	3	4.2	3	4.7	3	3.9
14	3	5.6	3	5.7	3	5.6	3	5.0	3	7.0
15	3	5.4	3	4.2	3	4.2	3	4.7	3	4.6
16	6	3.9	7	3.9	6	3.5	6	3.4	6	4.0
17	3	3.6	3	3.6	3	3.5	3	3.6	..	...
18	3	5.6	3	6.7	3	5.5	..	...	..	...
19	3	5.3	3	5.3	3	4.1	..	...	..	...
20	6	5.0	3	5.6	3	4.4	3	5.6	..	...
21	3	9.6	3	11.4	3	6.4	..	...	..	...
22	3	3.8	3	3.6	3	3.6	3	3.5	3	3.6
23	3	2.4	3	3.5	3	3.4	..	...	..	...
24	3	7.3	3	5.9	3	5.3	3	5.6	4	4.5
25	3	12.3	3	10.9	3	9.6	3	16.4	3	14.3
26	3	6.1	3	7.9	3	5.0	..	...	..	...
27	3	5.5	..	...	3	4.9	3	4.1	..	...
28	3	6.1	..	...	3	7.1	3	6.7	..	...
29	3	4.5	3	5.2	3	6.1	..	...	..	...
30	6	5.5	3	5.9	3	5.9	3	6.9	3	6.7
31	3	5.8	..	...	3	6.3	3	6.3	..	...
32	6	5.5	6	5.1	6	4.5	7	5.5	6	6.1
33	6	3.3	6	2.6	6	2.9	6	3.0	6	2.4
34	6	3.7	8	4.7	6	4.0	6	4.2	6	3.5
35	6	5.1	8	5.2	6	4.8	7	5.8	6	5.0
36	6	4.8	6	4.9	7	5.7	5	4.9	6	5.3
37	6	5.6	6	5.2	6	5.3	7	5.1	6	5.2
38	6	6.8	6	5.8	6	6.3	6	4.8	4	4.2
39	6	3.6	7	4.2	7	4.5	6	4.8	2	4.5
40	6	3.1	6	6.0	9	3.2	6	2.1	6	2.5
41	3	4.5	3	4.9	3	4.7	3	4.6	3	5.9
					Control Subjects					
1	6	5.2	6	6.3	6	4.7	7	5.6	7	7.9
2	3	4.9	3	4.9	4	4.4	4	5.0	4	6.9
3	6	3.9	6	3.7	6	3.8	6	3.7	3	5.7
4	6	3.5	6	3.0	5	2.7	2	3.2	9	5.3
5	6	4.0	7	4.5	6	3.1	6	4.5	6	6.5
6	6	4.0	6	3.5	6	2.5	6	3.4	6	6.2
7	6	4.8	12	6.3	6	4.7	..	...	7	7.2
8	3	4.4	3	4.7	3	4.1	3	6.5	3	7.2
9	3	6.5	3	5.6	3	4.7	3	5.6	3	8.1
10	6	4.7	6	5.9	6	4.4	6	6.4	6	8.6
11	3	4.8	3	4.3	3	4.5	..	...	..	...
12	3	5.7	..	...	3	6.3	3	5.1	..	...
13	3	5.9	3	5.9	3	7.8	3	5.3	3	5.6
14	3	5.4	3	5.7	3	5.0	3	5.4	3	7.1
15	3	5.4	..	...	3	4.9	3	6.2	..	...
16	3	4.3	3	5.1	3	6.3	..	...	..	...
17	3	7.3	3	7.5	3	5.3	..	...	..	...
18	3	4.5	3	5.1	..	...	..	...	..	...
19	3	6.0	3	6.4	3	5.3	3	5.9	3	7.2
20	3	12.4	3	12.1	3	9.8	3	16.3	3	10.9
21	3	5.4	3	5.4	3	4.8	3	5.1	3	5.5

periods there were very rapid respiratory rates (20 or more per minute) and of the cases in which there were very slow rates (10 or less per minute).

The mean respiratory rates for this group of persons were averaged for each period, and the corresponding mean values for the expiratory-inspiratory angles were likewise averaged. It is seen that the average value for the mean expiratory-inspiratory angle for the rapid rates varied only from 3.7 to 4.3 and that the average for the mean expiratory-inspiratory angles associated with the slow rates was considerably greater, varying from 6.0 to 8.3. If the relation between the rate and the mean expiratory-inspiratory angle were one of direct proportionality the product of the rate and the expiratory-inspiratory angle associated with it for all rates and all subjects would give a constant figure. Actually, this product as cal-

TABLE 15.—*Group Mean Expiratory-Inspiratory Angle During Each Period, Expressed in Scale Units*

Group	Number	Preliminary Period	First Pleasant Period	Unpleasant Period	Second Pleasant Period	Relaxed Period
All patients	41	5.3	5.6	4.8	6.0	5.5
Patients, group 1	29	5.5	5.8	4.8	6.6	6.0
Patients, group 2	12	4.7	5.0	4.8	4.8	4.7
Controls	21	5.4	5.7	5.0	5.8	7.1

TABLE 16.—*Relation Between Expiratory-Inspiratory Angle and Respiratory Rate, for Very Rapid and for Very Slow Rates*

	Respiratory Rates of More Than 20 per Min.			Respiratory Rates of Less Than 10 per Min.		
Period	Number	Average Rate	Average of Mean Angle	Number	Average Rate	Average of Mean Angle
Preliminary	5	23.4	4.3	8	8.4	7.5
First pleasant	6	24.3	4.0	12	8.5	7.1
Unpleasant	10	24.1	4.2	5	8.5	6.0
Second pleasant	7	24.7	4.0	12	8.2	8.3
Relaxed	2	23.4	3.7	14	8.2	7.9

culated from the individual values shown in tables 2 and 14 varies from about 30 to 130 and seems itself to be somewhat dependent on the rate, low values for the product being associated with low rates and, vice versa, high values for the product with high rates. Hence the relation between the mean expiratory-inspiratory angle and the rate of respiration cannot be one of simple inverse proportionality. The expiratory-inspiratory angle appears to be more nearly proportional to the square root or the cube root of the rate.

That the mean expiratory-inspiratory angle is not wholly determined by the respiratory rate is indicated by the observation that 2 persons may have the same respiratory rate, while the mean value for the expiratory-inspiratory angle is different in the 2 cases. For example, patient 15, during the second pleasant period, had a rate of 7 and a mean expiratory-inspiratory angle of 4.7, which is a rather sharp angle. Control subject 20, during the second pleasant period, had a similar rate of 7, whereas the mean expiratory-inspiratory angle was 16.3, which is a very broad, round angle. Patient 41, during the preliminary period,

was breathing at the rate of 9 per minute, and his mean expiratory-inspiratory angle was rather sharp, namely, 4.5. Patient 25, during the preliminary period, was breathing at the same rate, but his mean expiratory-inspiratory angle, 12.3, was round and broad. As a final example of this lack of correlation with rate, patient 41, during the first pleasant period, was breathing at the rate of 8 per minute, with a sharp mean expiratory-inspiratory angle, namely, 4.9. Patient 7, during the relaxed period, was breathing at the same rate per minute, and his mean expiratory-inspiratory angle was round, being 13.5.

The individual differences in the mean expiratory-inspiratory angles for the five periods are summarized for each group in table 17. This table is arranged like the other comparative tables.

Comparison of Two Pleasant Periods with the Preliminary Period and with Each Other.—For over half the patients of groups 1 and 2, the mean expiratory-inspiratory angle was displaced toward the broad side of the scale for the two pleasant periods as compared with the preliminary period. For both the pleasant periods the mean change in scale numbers was greater for group 1 than for group 2. The controls showed a comparable change in the expiratory-inspiratory angle in the comparison of the preliminary and the first pleasant period, but less than half showed a change in this direction for the second pleasant period as compared with the preliminary period. A shift of 2 scale divisions toward the broader angles for the second pleasant period as compared with the first appeared for 60 per cent of the subjects in group 1. It is of interest that table 4 shows no parallel slowing of respiratory rate for this comparison (comparison H).

Comparison of Unpleasant Period with the Preliminary Period, with the Two Pleasant Periods and with the Relaxed Period.—For group 1 and for the control group the mean expiratory-inspiratory angle was sharper for the unpleasant period than for the preliminary period, the two pleasant periods and the relaxed period. The mean value for the shift varied for group 1 from 1.2 to 2.7 scale divisions and for the controls from 0.8 to 2.6 scale divisions. For group 1 the greatest shift (2.7 scale divisions) occurred for the second pleasant period, whereas for the control group the greatest change (2.6 scale divisions) occurred for the relaxed period. The consistency of these changes, as indicated by the proportion of the group showing the change, was rather high, in each case being over two thirds of the group. For group 1 it ranged from 68 to 78 per cent, and for the controls, from 78 to 93 per cent. The large proportion (93 per cent) of the controls showing a marked difference between the unpleasant and the relaxed period is striking. The controls showed an equal degree of consistency in the change to slower rates of respiration for this comparison. Between 50 and 60 per cent of patients in group 2 had a sharper mean angle for the unpleasant period than for the two pleasant periods, and the same proportion of group 2 had a broader mean angle for the unpleasant period than for the preliminary and the relaxed period.

Comparison of the Relaxed Period with the Preliminary Period and with the Two Pleasant Periods.—The patients of group 1 showed no consistent shift in the mean expiratory-inspiratory angle when the preliminary period was compared with the relaxed period (comparison G). They showed a shift toward sharper angles for the relaxed period as compared with the pleasant periods. Table 4 shows no comparable change in the rate of respiration for these comparisons (comparisons D and I, group 1). The patients of group 2 showed no significant or consistent change in the mean expiratory-inspiratory angle for any of the comparisons involving the relaxed period.

TABLE 17.—*Summary of Changes in Expiratory-Inspiratory Angle on Comparison of Various Periods*

Comparison of Two Periods	Groups of Subjects	No. in Group	1 Subjects Showing Increase During Second Period				2 Subjects Showing Decrease During Second Period				3 Subjects Showing No Change	
					Increase in Mean Expiratory-Inspiratory Angle				Decrease in Mean Expiratory-Inspiratory Angle			
			No. of Subjects	Percentage of Group	Mean	Range	No. of Subjects	Percentage of Group	Mean	Range	No. of Subjects	Percentage of Group
A Preliminary and first pleasant period	Total number of patients	36	20	56	1.2	0.1-7.2	13	36	0.8	0.1-1.7	3	8
	Group 1	25	13	52	1.4	0.1-7.2	9	36	0.9	0.1-1.7	3	12
	Group 2	11	7	64	0.8	0.1-2.9	4	36	0.6	0.4-1.0	0	0
	Controls	19	10	52	0.7	0.2-1.5	6	32	0.5	0.2-0.9	3	16
B First pleasant and unpleasant period	Total number of patients	38	9	24	0.5	0.1-1.1	26	68	1.4	0.1-9.3	3	8
	Group 1	27	4	15	0.7	0.2-1.1	21	78	1.5	0.1-9.3	2	7
	Group 2	11	5	45	0.4	0.1-0.8	5	45	0.9	0.2-2.8	1	10
	Controls	18	4	22	0.9	0.1-1.9	14	78	1.2	0.3-2.3	0	0
C Unpleasant and second pleasant period	Total number of patients	34	23	68	2.0	0.1-9.1	11	32	0.5	0.1-1.5	0	0
	Group 1	22	16	73	2.7	0.1-9.1	6	27	0.4	0.1-0.8	0	0
	Group 2	12	7	58	0.5	0.1-1.0	5	42	0.7	0.1-1.5	0	0
	Controls	16	13	81	1.4	0.3-6.5	3	19	1.3	0.1-2.5	0	0
D Second pleasant and relaxed period	Total number of patients	27	10	37	0.7	0.1-2.0	17	63	1.3	0.1-6.1	0	0
	Group 1	16	5	31	0.9	0.1-2.0	11	69	1.7	0.1-6.1	0	0
	Group 2	11	5	45	0.6	0.1-1.3	6	55	0.5	0.2-0.8	0	0
	Controls	14	13	93	1.7	0.3-2.8	1	7	5.4		0	0
E Preliminary and unpleasant period	Total number of patients	39	13	33	0.7	0.1-1.6	25	64	1.1	0.1-3.2	1	3
	Group 1	27	6	22	0.9	0.2-1.6	20	74	1.2	0.1-3.2	1	4
	Group 2	12	7	58	0.5	0.1-0.9	5	42	0.5	0.3-1.0	0	0
	Controls	20	3	15	1.5	0.6-2.0	17	85	0.8	0.1-2.6	0	0
F Preliminary and second pleasant period	Total number of patients	31	19	61	1.6	0.1-7.9	10	32	0.9	0.3-2.0	2	7
	Group 1	19	12	63	2.2	0.3-7.9	6	32	0.9	0.3-1.7	1	5
	Group 2	12	7	58	0.6	0.1-1.4	4	33	1.0	0.3-2.0	1	9
	Controls	16	7	44	1.4	0.1-3.9	8	50	0.5	0.1-0.9	1	6
G Preliminary and relaxed period	Total number of patients	25	13	52	1.5	0.1-7.4	12	48	0.9	0.1-2.8	0	0
	Group 1	14	8	57	1.9	0.1-7.4	6	43	1.0	0.1-2.8	0	0
	Group 2	11	5	45	0.9	0.5-1.4	6	55	0.8	0.1-2.6	0	0
	Controls	22	13	87	2.1	0.1-3.9	2	13	0.9	0.3-1.5	0	0
H First pleasant and second pleasant period	Total number of patients	31	17	55	1.7	0.2-6.3	11	35	0.8	0.1-3.9	3	10
	Group 1	20	12	60	2.2	0.2-6.3	6	30	0.5	0.1-1.1	2	10
	Group 2	11	5	45	0.6	0.4-1.0	5	45	1.2	0.1-3.9	1	10
	Controls	14	5	36	1.4	0.1-4.2	6	43	0.4	0.1-0.7	3	21
I First pleasant and relaxed period	Total number of patients	27	15	56	1.1	0.1-5.8	10	37	1.6	0.2-6.3	2	7
	Group 1	16	10	63	1.4	0.1-5.8	5	31	1.9	0.3-6.3	1	6
	Group 2	11	5	45	0.7	0.3-1.0	5	45	1.3	0.2-3.5	1	10
	Controls	15	13	87	1.8	0.1-2.7	2	13	0.8	0.3-1.2	0	0
J Unpleasant and relaxed period.	Total number of patients	27	15	56	1.8	0.2-6.8	9	33	0.6	0.1-2.1	3	11
	Group 1	16	11	68	1.9	0.2-6.8	3	19	0.4	0.1-0.8	2	13
	Group 2	11	4	36	1.0	0.2-1.6	6	55	0.7	0.1-2.1	1	9
	Controls	15	14	93	2.6	0.7-4.2	1	7	2.2		0	0

The controls showed an appreciable shift toward broader angles for the relaxed period as compared with the preliminary period and the two pleasant periods (comparisons D, G and I). The shift ranged from 1.7 to 2.1 scale divisions, and was shown by from 87 to 93 per cent of the subjects. The proportion of the controls showing a parallel retardation in respiratory rate was much lower, namely, 47 to 66 per cent.

Summary.—The patients of group 1 and the controls had a sharper mean expiratory-inspiratory angle for the unpleasant period than for the four other periods. For about two thirds of group 1 the mean expiratory-inspiratory angle for the second pleasant period was broader than for the four other periods, and for this group the respiratory rate was also slowest during this period. The patients in group 2 showed no outstanding changes in the mean expiratory-inspiratory angle. There was a

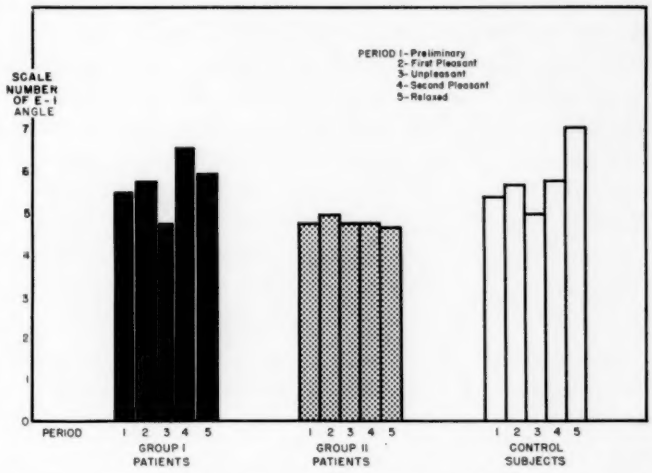

Fig. 17.—Chart showing group averages of individual mean expiratory-inspiratory angles during each period for patients of group 1, for patients of group 2 and for the control subjects.

slight tendency for these patients to have a sharper angle for the preliminary period than for the four other periods. When tables 4 and 17 are compared it appears that a shift in the mean expiratory-inspiratory angle does not always correlate closely with a change in respiratory rate.

COMMENT

Literature.—Earlier investigators, working in Wundt's laboratory, used a small number of normal subjects to study in detail the effect of pleasant ideas, of unpleasant ideas and of tension states on various aspects of respiration over short periods. Mosso [2] and Minne-

man [23] found no correlation between the respiration and the type of emotion experienced. Zoneff and Meumann [5] observed acceleration of respiration during the pleasant period and slowing during the unpleasant period. This contrasts with the observation of Mentz [3] of slower breathing during the pleasant than during the unpleasant period.

The studies reported in the present paper indicate that during unpleasant thoughts the respiration is apt to be more rapid than during pleasant thoughts (see Mentz). On the other hand, these studies include a few cases in which the opposite effect was shown and a number in which no change in rate occurred. The acceleration during the unpleasant thoughts appears to be less marked for so-called normal subjects than for psychoneurotic patients with conditions diagnosed as hysteria, anxiety neurosis and phobia. Little or no significant change in rate was observed for psychoneurotic patients with conditions diagnosed as hypochondriasis, compulsion neurosis and reactive depression.

With regard to depth of respiration, Lehmann [1] found deep breathing during both pleasant and unpleasant affects, but observed that the unpleasant affects were associated with greater irregularity in breathing. Rehwaldt,[4] Zoneff and Meumann [5] and Feleky [6] all noted shallower breathing during pleasant than during unpleasant or tense states.

The present studies indicate great individual variability in the changes in depth of respiration. The depth of respiration tended to be somewhat greater during the unpleasant period for the patients of the first diagnostic group and, to a smaller extent, for the controls (see Rehwaldt, Zoneff and Meumann and Feleky). At the same time, a few showed no change, and an appreciable number reacted by shallower breathing during the unpleasant period (see Mentz). The psychoneurotic patients of the second diagnostic group showed very slight changes, some in the direction of deeper breathing during the unpleasant period and some in the direction of deeper breathing during the pleasant period. Many showed no change.

From the variability shown by the patients and controls in the results presented here, it seems that one cannot generalize from a few cases regarding the effect of pleasant and unpleasant ideas on rate and depth of respiration. There may be a tendency for unpleasant ideas to be accompanied by more rapid and deeper breathing; some persons, however, show little or no change; some subjects have more rapid but shallower breathing while experiencing unpleasant emotions, and some may react by deeper but slower respirations. When a large enough series of cases is considered, such a lack of agreement as occurred among the previous investigators becomes clarified.

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23. Minneman, E., cited by Rehwaldt.[4]

A more consistent correlation between emotional state and respiration becomes evident when the changes in minute respiratory volume, rather than the changes in the component respiratory functions, rate and depth, are followed. An association between hyperventilation and feelings of distress is known to exist in hyperventilation tetany. In the literature on respiration in relation to emotion there seems to be no other available information on minute respiratory volume or data on rate and depth of respiration in sufficient detail to enable one to calculate the total ventilation. The studies presented here show that about 90 per cent of the control subjects and of the psychoneurotic patients of the first diagnostic group had a greater minute respiratory volume during the unpleasant period than during the preliminary period and that between 85 and 95 per cent of these two groups of subjects had a somewhat lower minute respiratory volume during the two pleasant periods than during the unpleasant period. The changes were quantitatively greater for the patients of group 1 than for the controls, and for some individual patients the difference between the low value for ventilation for the pleasant period and the high value for the unpleasant period amounted to over 7 liters per minute. An increase in minute respiratory volume during the unpleasant period as compared with the two pleasant periods was shown by 90 per cent (first pleasant period) and by 75 per cent (second pleasant period) of patients in group 2, but the mean increase in minute respiratory volume for these patients was only 0.6 liters, as compared with a mean increase of over 3 liters shown by most of the patients of group 1. The patients in group 2 showed no appreciable difference in ventilation between the preliminary and the unpleasant period. There did, however, appear to be a slight decrease in ventilation for the two pleasant periods as compared with the preliminary period. The difference involved was again small.

An increase in oxygen consumption was found by Ziegler and Levine [10] in 12 of 14 psychoneurotic war veterans to whom an unpleasant war experience was suggested. In 1 case the increase amounted to 27 per cent. Two of these patients showed a decrease in oxygen consumption. No normal controls were used. Gräfe and Mayer [24] showed in 10 patients an average increase in metabolism of 7.6 per cent during hypnotic anxiety as compared with hypnotic sleep. Preliminary measurements preceding the experimental situation were not reported, and, again, normal control subjects were not used. Landis,[7] in a careful study on himself and 2 other subjects, showed that an emotional disturbance caused by electrical stimulation slowed the metabolic rate in 2

24. Gräfe, E., and Mayer, L.: Ueber den Einfluss der Affekte auf dem Gesamtstoffwechsel: Untersuchungen in der Hypnose, Ztschr. f. d. ges. Neurol. u. Psychiat. **86**:247, 1923.

of the 3 subjects by 8 and 4 per cent, respectively. Landis also reported in the same paper that anger "is sometimes accompanied by an increase in metabolism and at other times by a decrease."

In the present studies, 63 per cent of the psychotic patients in group 1 and only 39 per cent of the normal controls showed an increase in metabolism during the unpleasant period as compared with the preceding pleasant period, and 15 per cent of group 1 and 28 per cent of the controls showed no change. The other subjects in these groups showed changes in the opposite direction. About half the subjects showed an increased metabolic rate for the unpleasant as compared with the preliminary period. About two thirds of the patients had a lower metabolic rate for the pleasant periods than for the preliminary period. This shift did not appear for a majority of the controls. These results seem to accord with those of Ziegler and Levine [10] for psychoneurotic patients and with those of Landis [7] for normal controls. In evaluating the metabolic changes found in the present studies, it should be emphasized that the estimation of oxygen consumption from metabolism records over periods which in many cases lasted only three minutes is bound to involve greater inaccuracies than does the measurement of rate and depth of respiration by this method. Nevertheless, the changes in oxygen consumption shown in the present studies indicate the need for more rigorous measurement of oxygen consumption under changing ideational stimuli. It is possible that the discrepancies found in repeated records of patients during basal metabolism tests may be accounted for by changes in the ideational content and emotional state of the patients.

Types of Ideas Present.—During the preliminary period the ideas reported by all the subjects were of a casual nature. The uniformity of the ideas reported by all groups for the pleasant period and the consistent inactivity that characterized these ideas have been noted. Since none of the subjects reported pleasant ideas connected with physical activity or with erotic fantasies or memories, it appears that the nature of the experimental setup was conducive to the appearance of these quiet, relaxing ideas when the suggestion "pleasant ideas" was made by the investigator. It is probable that erotic ideas associated with pleasant affect were present in some cases, but were not reported. There were no characteristic distinctions between the reports of the patients of both groups and the reports of the controls for the pleasant periods.

The uniformity of content that characterized the reports of the subjects for the pleasant periods was less evident for the unpleasant period. There was, however, for the unpleasant period some uniformity in the feeling described. The suggestion of unpleasant ideas provoked ideas of a type that are better described as upsetting or disturbing. The patients characteristically referred to fears, to accidents or acts of vio-

lence, to cruel fantasies or to symptoms. In contrast to the patients, the controls characteristically referred to realistic, everyday problems, worries and aggravations. There seems to have been some difference in the types of emotions reported by the two groups of patients. Ideas of violence and fears were prominent in the reports of a larger proportion of patients in group 1 than of those of group 2, whereas somatic complaints and a feeling of dejection were prominent in the reports of a larger proportion of patients in group 2 than of those in group 1.

There was considerable uniformity in content and feeling tone during the relaxed period. The idyllic fantasies or memories that characterized the first pleasant period were not present. The patients seemed to be concerned with the process of relaxing, which to many seemed synonymous with trying to fall asleep. None reported having actually fallen asleep, and, as far as one could observe, none really did go to sleep.

There may be some ambiguity in the use of the terms "pleasant period" and "unpleasant period." The second and fourth periods are referred to as "pleasant" because during these periods the words "pleasant ideas" were used as the verbal stimulus. Analysis of the reports given by the patients and the control subjects indicates that the feeling tones present are not properly described by the stimulus word. It would be more accurate to qualify the term "pleasant" by such terms as "peaceful," "restful," "quiet," "relaxing" or "inactive." The third period is referred to as "unpleasant," again, because the words "unpleasant ideas" were used as the verbal stimulus. The reports of the patients and control subjects can be described more adequately by such qualifying terms as "upsetting" or "disturbing."

Unconscious Ideas.—The changes in the various aspects of the respiratory function in the present paper are studied in relation to the conscious, verbally expressed moods and ideas of the subjects. It is of additional interest to inquire to what extent the respiratory functions may have been influenced by ideas and impulses that were repressed and of which the subject was therefore not conscious. These ideas may have been different in tone and content from the conscious material. It is conceivable, for example, that during a pleasant period a subject might be drawn to some highly charged association related to a chain of repressed memories. The effect of this unconscious material might be perceived as anxiety, or it might appear merely as mental blocking or lethargy, and hence be wholly absent from the patient's report. It is also conceivable that the response to fearful or unpleasant ideas might be different for a patient for whom these ideas provide a deep masochistic satisfaction than for a subject in whom fearful ideas awaken mainly fear and the desire to escape. However, since the patients and controls included in the present study were not psychoanalyzed, it would be idle

to speculate on the nature of the unconscious trends and fantasies present in the individual cases and on the possible effect of such unconscious material on the respiratory tracings.

Reliability of the Subjective Material.—In considering experiments on emotional factors in respiration, it is necessary to evaluate the reliability of the subjective material. In the present experiments this material was obtained from the verbatim reports of the patients and controls, as recorded immediately after the tests. These reports might differ from the actual mental content during the tests, owing to difficulty in remembering on the part of the patient or control, to indifference on his part, to a desire to give the investigator the answer he sought or even to malingering.

With regard to errors due to forgetting, none of the subjects reported having any difficulty in recalling the ideas that had been in mind during the five successive periods. These ideas were, in most cases, similar to or identical with the ideas that the subject had mentioned before the start of the respiratory test as being associated with pleasant feelings, on the one hand, or with unpleasant feelings, on the other.

The disturbing effect of indifference or apathy on the part of the subject was minimized by having the initiative for the ideas come from the subject rather than from the investigator and by avoiding leading questions or questions which could be answered by a casual "yes" or "no." When questioned after the tests as to what had been in their minds during the test periods, all the subjects made some concrete statement. None evaded the questions by replying "I don't know," or "I don't care to say." It is conceivable that the rapport between the investigator and the subjects played a role in evoking this degree of cooperation, and thus acted as a form of indirect suggestion.

Evidence as to the role of malingering or of an overzealous desire to comply seemed to be available from the actual material reported by the subjects. This material was strikingly and unexpectedly uniform, especially for the pleasant period, for which the experimental setup seemed to have evoked a common pattern of ideational response. If the replies of even a few of the patients had represented faking or bluffing it is hard to conceive that they would have conformed so closely to a common pattern. The fact that the reports for the unpleasant period were never casual, but were of a personal nature and appeared to be upsetting, again lends support to the assumption that conscious distortion of the reports occurred only infrequently.

Additional evidence as to the reliability of some of the reports comes from statements regarding difficulties encountered in following the instructions. Several patients reported that pleasant ideas did not immediately replace the unpleasant ideas during the second pleasant period.

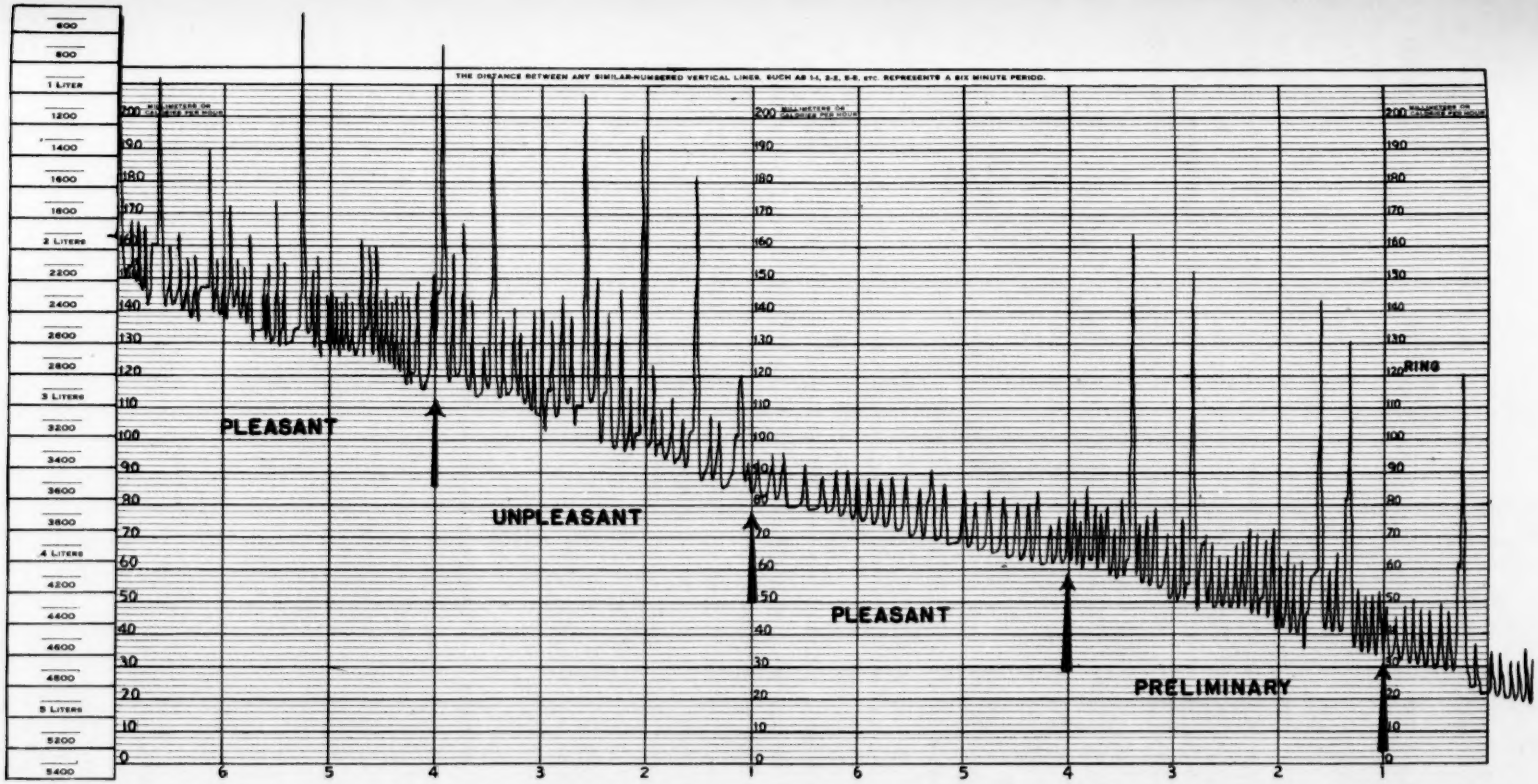

Fig. 18.—Continuous record of experiment on patient 7. The duration of each period was three minutes. During the second pleasant period the patient stated that pleasant ideas did not come to mind because she was so upset during the unpleasant period.

One subject (patient 7) reported that pleasant ideas did not return at all during the period that followed the unpleasant period. This report is especially significant since, as can be seen from figure 18, the respiratory tracing for the second pleasant period in this case resembles that for the unpleasant period and contrasts strikingly with the tracing obtained during the first pleasant period, for which the patient reported having experienced pleasant ideas.

Some subjects offered additional evidence as to the nature of the emotional tone during the various periods. During the unpleasant period a great many subjects showed evidence of increased muscular tension, tremors, restlessness, pallor, sweating, sighing and even tears. During the pleasant periods the patients frequently closed their eyes and appeared relaxed. On the whole, it seems reasonable to assume that while, obviously, all the ideas that had been present were not covered in the reports obtained from the subjects, nevertheless these reports represent a fairly reliable sample of the ideas that had been present.

Sleep as a Disturbing Factor.—The possibility that some of the patients and controls might have fallen asleep during the tests, especially during the pleasant and the relaxed periods, was taken into consideration. Many of the patients closed their eyes during one or both of these periods. Changes in the level of consciousness were reported, especially during the pleasant and the relaxed periods. Patients reported feeling relaxed, being somewhat drowsy, feeling as if they were ready to go to sleep. Yet all the subjects replied in the negative when questioned routinely at the end of the tests as to whether they had been asleep. In 5 experiments the subjects were told to press a signal in response to an auditory stimulus given at intervals during the test. In these tests the rapidity and accuracy of the response indicated that the subjects had not been asleep during any part of the test. These subjects and those who kept their eyes open during the pleasant and the relaxed periods and demonstrated that they were awake by blinking or otherwise moving their eyes showed essentially the same changes in the respiratory tracings as did the patients who kept their eyes closed for the pleasant and relaxed periods. It seems reasonably certain, therefore, that the changes measured during the pleasant and relaxed periods were not changes in respiration associated with sleep. Other respiratory records have been obtained during natural sleep. These will be presented in another communication.

Group Differences.—The group differences that appeared in the respiratory response call for comment. As has appeared from analysis of the results, the patients in group 1 reacted most intensely and those in group 2 least of all. When mean values for each group are used to indicate respiratory reactivity, the well defined maxima for rate and

minute respiratory volume that appeared during the unpleasant period for group 1 and for the controls, and which were relatively more pronounced for group 1, were lacking for group 2. Several different interpretations of the difference can be postulated. It is possible that with regard to changes in processes involving the autonomic nervous system patients with hypochondriasis, with reactive depression or with compulsion neurosis tend, in general, to be less reactive than are normal persons, and that normal persons are in this respect less reactive than patients with hysteria, with phobias or with anxiety neurosis. In this connection, Whitehorn, Kaufman and Thomas [25] found that patients with involutional melancholia showed signs of strong affect (laments, hand wringing) without acceleration of heart rate. Whitehorn and Richter [26] found that during interviews a group of psychoneurotic patients showed greater so-called beat to beat variability of the heart rate [27] than did a group of control subjects, who, in turn, showed greater variability than did a group of psychotic patients. It might be fruitful to study in greater detail psychoneurotic patients with diagnoses similar to those in group 2 to determine whether the lack of reactivity observed here for the respiratory responses hold also for cardiac and other types of response. It is possible that from the standpoint of responses involving the autonomic nervous system these patients react more like psychotic patients than like psychoneurotic patients in this diagnostic group 1. This would be of interest in regard to the theory that relates hypochondriasis dynamically to the psychoses (Freud [28]).

It is, of course, conceivable that the lack of respiratory reactivity of patients in group 2 was due to a relative lack of affect. It is also possible that in the case of patients of group 2 the respiratory pattern was influenced primarily by some consistent predominating mood, which could not be shifted from period to period by the suggestions of the investigator and of which the patient may have been unaware. These speculations are advanced only tentatively, pending further experimental investigation.

In the present studies, of 41 psychoneurotic patients the majority (29) belonged to diagnostic group 1. Hence the results for all the patients, taken as a single group, appear to resemble those for the reactive group 1. It is not likely that quite the same statistical distribution would hold for unselected groups of psychoneurotic patients.

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25. Whitehorn, J. C.; Kaufman, M. R., and Thomas, J. M.: Heart Rate in Relation to Emotional Disturbances, Arch. Neurol. & Psychiat. **33**:712 (April) 1935.

26. Whitehorn, J. C., and Richter, H. G.: Unsteadiness of the Heart Rate in Psychotic and Neurotic States, Arch. Neurol. & Psychiat. **38**:62 (July) 1937.

27. Percentage variation in the duration of successive individual heart beats.

28. Freud, S.: Hemmung, Symptom und Angst, in Gesammelte Schriften, Vienna, Internationalen Psychoanalytischen Verlag, 1928, vol. 11, p. 89.

Since the number of patients in group 2 was only 12, further studies with larger numbers of patients are especially desirable and are necessary before these results can be used for purposes of differential diagnosis.

SUMMARY

1. Respiratory tracings were made on a series of 41 psychoneurotic patients and 21 control subjects during tests lasting from a quarter of an hour to half an hour and comprising five successive periods. During the second, third and fourth periods, respectively, the subjects were directed to think of pleasant, of unpleasant and, again, of pleasant ideas. During the first period no directions were given, and during the last period the subjects were asked to relax.

2. At the completion of each respiratory tracing the subject was asked to state the ideas that had been present during each of the five periods. In all cases indifferent casual topics were reported for the preliminary period; quiet, restful ideas, usually connected with rural scenes, were reported for the first, and in most cases for the second, pleasant period; disturbing and upsetting ideas, memories and symptoms were reported for the unpleasant period, while during the relaxed period the subjects reported having been concerned with the process of relaxing and with ideas of going to sleep.

3. The respiratory tracings were analyzed period by period for rate, depth, minute respiratory volume, metabolic rate and spread of the expiratory-inspiratory angle.

4. It was found that of the psychoneurotic patients, those having conditions diagnosed as hysteria, phobia or anxiety neurosis (29 patients, referred to as group 1) reacted as a group with pronounced respiratory changes. The remaining patients, whose conditions were diagnosed as hypochondriasis, reactive depression or compulsion neurosis (12 patients, group 2) reacted as a group with very slight respiratory changes, and frequently with no changes at all. The controls reacted less than the patients of group 1 and more than the patients of group 2.

5. For each group of subjects the mean values for rate, depth and minute respiratory volume were practically the same for the two pleasant periods, and in most cases were slightly lower for these two periods than the corresponding group value for the preliminary period. The mean values for the metabolic rate were less constant for the two pleasant periods, but the group values for both pleasant periods were lower than the corresponding value for the preliminary period; the values for the two pleasant periods were higher (broader angles) than the value for the preliminary period.

6. In a comparison of the unpleasant period and the two pleasant periods, the patients in group 1 showed a striking increase in the mean values for the rate, depth and minute respiratory volume, as well as some sharpening of the expiratory-inspiratory angle. The patients of group 2 showed no significant change in the mean values for the rate and the expiratory-inspiratory angle, and only a slight increase in the mean depth and minute respiratory volume for the unpleasant period.

7. The most consistent changes were observed for the minute respiratory volume. Between 86 and 96 per cent of the patients in group 1 and of the controls showed a considerable increase in minute respiratory volume for the unpleasant period as compared with the two pleasant periods, and for the same comparisons over 75 per cent of patients in group 2 showed a very slight increase in minute respiratory volume. About 90 per cent of patients in group 1 and of the controls had a higher minute respiratory volume during the unpleasant than during the preliminary period. For this comparison no consistent change was shown by patients in group 2. All the patients in group 1 and over 90 per cent of the controls showed a marked decrease in minute respiratory volume during the relaxed as compared with the unpleasant period.

8. The lowest mean rate (11.7 respirations per minute) and the broadest mean expiratory-inspiratory angle (7.1 scale divisions) were those for the control group during the relaxed period. The lowest mean minute respiratory volume (5 liters) was that for the control group during the two pleasant periods and the relaxed period. The largest mean values for rate (17.3 respirations per minute), for depth (653 cc.), for minute respiratory volume (8.4 liters per minute) and for metabolic rate (+ 1 per cent) were those of patients in group 1 during the unpleasant period.

SUMMARY OF CASE HISTORIES

CASE 1.—A. M., a 30 year old housewife, married, white, native-born, was transferred from the medical service, complaining of episodes of palpitation and pain in the region of the heart, of approximately ten years' duration. On admission she was tense and restless. There were a slight pulmonic systolic murmur, hyperactive knee jerks, fine lateral nystagmus movements and a marked red streak on stroking the skin. The electrocardiogram was normal. There was a questionable diagnosis of syphilis.

The diagnosis was anxiety neurosis and malnutrition.

CASE 2.—C. B., a 33 year old housewife, married, white, native-born, complained of vomiting for the last seven years. There was a history of having taken bromides for months. Physical examination showed slight blurring of the nasal margins of the optic disks; the corneal reflexes were diminished bilaterally; the gag reflex was very active; the deep reflexes were hyperactive. The patient

fell backward in the Romberg position. On admission the bromide content of the blood was 175 mg. per hundred cubic centimeters.

The diagnosis was hysteria and bromidism.

CASE 3.—M. H., a 23 year old housewife, married, white, native-born, was transferred from the medical service, complaining of attacks of palpitation, substernal pain, dyspnea, choked feeling and general weakness. The symptoms were of eight months' duration and had started in connection with the patient's first pregnancy, but had become much intensified after her delivery. Physical examination gave normal results except for a blowing apical systolic murmur. The electrocardiogram was normal.

The diagnosis was anxiety neurosis.

CASE 4.—P. R., a 37 year old housewife, married, white, native-born, was admitted from the outpatient department complaining of palpitation, weakness, dizziness, substernal pain and vomiting. She felt uncomfortable in crowds or elevators. The symptoms were of two years' duration. Physical examination gave normal results except for tremor of the outstretched hands. The electrocardiogram was normal.

The diagnosis was anxiety neurosis.

CASE 5.—This case is described in the text.

CASE 6.—A. R., a 40 year old, white, native-born woman worker, separated from her husband, complained of headache, nausea and vomiting and inability to walk. The symptoms were of one month's duration and followed a fall on her back and head. Physical and neurologic examinations gave normal results. Roentgenograms and examination of the spinal fluid revealed nothing abnormal.

The diagnosis was hysteria.

CASE 7.—F. C., a 30 year old married woman, white, native-born, was transferred from the Boston Lying-In Hospital because of development of symptoms during pregnancy. The symptoms consisted of extreme irritability, vague fears that something was going to happen, fear of high places, crawling sensations over the right side of the scalp, feeling of wind rushing through the head, jumping and palpitation of the heart, nightmares and mild depression. Since the last pregnancy the patient had avoided sexual relations through fear of having another child. Physical and neurologic examinations gave normal results.

The diagnosis was anxiety neurosis.

CASE 8.—L. H., a 31 year old gardener, white, single, native-born, had complained of nervousness and anxiety for seventeen years. When anxious, he did not sleep well, was tense and "jittery" and had palpitations and shortness of breath. The symptoms followed influenza, when the patient was 14, and became worse at the age of 18, at which time he had occasional asthmatic attacks. Some of the anxiety attacks came on after masturbation; other attacks were described as occurring without any precipitating factor.

The diagnosis was anxiety neurosis.

CASE 9.—A. S., a 31 year old, married Jewish housewife, complained of morning vomiting, palpitation and crying spells. She had had feelings of discomfort in the genitalia for the past one and a half years. Since hysterectomy, one and

one-half years before, she had had episodes of vomiting and palpitation. Physical examination revealed essentially a normal condition. The basal metabolic rate was —5 per cent.

The diagnosis was anxiety neurosis.

CASE 10.—This case is described in the text.

CASE 11.—This case is described in the text.

CASE 12.—This case is described in the text.

CASE 13.—A. Z., a 21 year old woman, single, white, native-born, a nurse, complained of episodes of palpitation, "jitters" tremor, feeling upset and desire to cry, of eighteen months' duration. Physical examination gave essentially normal results except for hyperactive reflexes, which were equal on the two sides.

The diagnosis was anxiety neurosis.

CASE 14.—E. S., a 33 year old woman, single, native born, complained of nausea, vomiting, headache and amenorrhea, of two years' duration. Symptoms came on after sexual experiences and lasted from two to three months, with spontaneous recovery. The patient had a recurrence after each sexual experience. Physical examination revealed nothing abnormal except for a basal metabolic rate of — 30 per cent, which was improved by thyroid medication. No other endocrine disturbance was found after repeated careful examinations and a long period of observation.

The diagnosis was hysteria.

CASE 15.—J. V., a 33 year old white man, native-born, single, a college graduate, complained of his heart pounding and of shortness of breath, faintness and fear that he was going to die. In addition, during the attacks he described dizziness, weakness in his knees and a feeling of fulness in the upper part of the abdomen. These attacks were of four years' duration. They usually came on when he tried to walk alone, drive his car alone or go on a train alone. Physical and neurologic examinations revealed nothing abnormal. The pulse was 70, and the blood pressure was 140 systolic and 80 diastolic. The basal metabolic rate was —23 per cent.

The diagnosis was anxiety neurosis; phobias.

CASE 16.—T. H., a 21 year old man, single, white, native-born, a gravedigger, complained of lack of concentration, palpitation, cardiac difficulties and fear that his heart would stop and that he was going to die. These ideas forced themselves on his attention, and he became more and more upset. When upset, he felt that all was not right; he was agitated and believed that something was wrong with his stomach. Physical examination and lumbar puncture revealed nothing abnormal. A gastrointestinal series of roentgenograms and electrocardiogram were essentially normal. The basal metabolic rate was + 7 per cent.

The diagnosis was anxiety neurosis and reactive depression (?).

CASE 17.—R. S., a 17 year old girl, unmarried, white, native-born, complained of a marked tremor in the right leg and pain in the back, of fifteen months' duration, following a fall in which she twisted her back. In addition, there were marked spasms of the legs, in which they were drawn up. After the fall the legs were put in casts, during which time the patient suffered acute pain in her back. Physical examination showed marked tremor of the right leg, with a rate of 7 per second, which increased on emotional excitement, and muscular spasm of the right leg. Flexion of the thigh on the hip caused pain in the back; there was tender-

ness on light palpitation over the third and fourth lumbar and fifth sacral vertebrae and the sacroiliac junction. There were questionable hypesthesia over the right leg and foot, marked, irregular clonus of the right ankle, slight clonus of the left ankle, pronounced blushing and sweating of the hands.

The diagnosis was hysteria.

CASE 18.—M. S., a 24 year old woman worker, white, single, native-born, complained of laughing, crying and fatigability, of several months' duration. She had always been frigid and showed a marked tendency toward dramatization. She had considerable push of speech and talked freely about her intimate affairs. Physical examination revealed nothing abnormal.

The diagnosis was hysteria.

CASE 19.—E. D., a 34 year old housewife, white, married, native-born, complained of sharp pains in the back, dizziness, substernal pressure in the chest, and pounding of the heart, of three years' duration. She also complained of marked fears of her mother's death and of the death of her adopted child and had swings in mood, lasting several hours. Physical examination showed marked obesity, the patient having gained 40 pounds (18.1 Kg.) in weight since her marriage, seven years ago. The left pupil was irregular; the deep reflexes were hyperactive.

The diagnosis was anxiety neurosis and phobia.

CASE 20.—F. C., a 54 year old woman, white, married, a social worker, complained of diarrhea, of one year's duration, faintness, palpitation and dizziness. She had had three or four episodes of loss of consciousness, weakness and palpitation. Physical examination showed generalized, coarse tremor of the arms and legs during emotional tension. The reflexes were hyperactive. The basal metabolic rate was —11 per cent. A barium sulfate enema showed the sigmoid colon to be slightly narrowed. Proctoscopic examination showed acute injection of the mucosa and a finely wrinkled surface.

The diagnosis was hysteria and mucous colitis.

CASE 21.—C. D., a 29 year old man, single, white, native-born, complained of episodic palpitation, shortness of breath, hot flashes and blood rushing into his head, of six years' duration. In addition, there were tingling and numbness in the calves and the lower part of spine. Attacks came on when he was emotionally upset. The blood pressure was 144 systolic and 86 diastolic. Physical examination gave normal results.

The diagnosis was anxiety neurosis.

CASE 22.—P. A., a 38 year old Italian laborer, married, was transferred from the medical service, complaining of epigastric pain, vomiting and tremor, of eight years' duration. Pain was present when the patient was angry or upset. He occasionally noticed his heart beating fast. Physical examination showed hyperactive deep reflexes. The basal metabolic rates were + 14, — 9 and — 15 per cent. The gastrointestinal series of roentgenograms showed a questionable hiatus hernia in the cardia of the stomach.

The diagnosis was anxiety neurosis, with hysterical features.

CASE 23.—F. A., a 23 year old Italian schoolteacher, single, complained of weakness of the face and extremities and fleeting paralysis of the extremities, most

marked in the right leg. The left hand and forearm were held in contracture. The patient also mentioned palpitation, being upset and feelings of inadequacy. Physical examination showed obesity; contracture of the left hand, forearm and arm, and anesthesia to pain and touch in the left hand, forearm and arm and the left foot, leg and thigh. The gait dragged; the left leg "drew weight." Lumbar puncture revealed nothing abnormal. Sugar tolerance was normal. The basal metabolic rate varied from — 15 to + 15 per cent.

The diagnosis was hysteria.

CASE 24.—M. E., a 19 year old woman, white, native-born, a college student, complained of tension, "jitters," "feelings of something being wrong" and occasional palpitation, of two months' duration. The onset was connected with school examinations and feelings of inadequacy in her studies. Episodes of crying were associated with mild feelings of depression. Physical examination gave normal results.

The diagnosis was anxiety neurosis.

CASE 25.—M. B., a 26 year old woman, white, single, native-born, a social worker, complained of nausea, occasional vomiting and difficulties in adjustment, of two years duration. There were occasional episodes of palpitation and shortness of breath. She had symptoms on meeting people, especially in relation to social and intimate situations with men. Physical examination revealed essentially normal conditions except for hyperactive deep reflexes.

The diagnosis was hysteria, with some anxiety features.

CASE 26.—M. M., a 21 year old woman, single, white, native-born, complained of nervousness, of four years' duration. There were swings in mood. When depressed she had pain in her stomach and right leg. At times she dragged the right leg. There were phobias of going in crowds and of going up and down stairs. Physical examination, including an electrocardiogram, revealed nothing abnormal.

The diagnosis was hysteria.

CASE 27.—A. A., a 27 year old housewife, white, married native-born, complained of hypertension, headaches, dizziness, depression, nausea, vomiting and feelings of anxiety, of five years' duration. Physical examination showed a blood pressure of 220 systolic and 150 diastolic, slight enlargement of the heart to the left and systolic murmur at the apex. Examination of the fundi showed obliteration of the margins of the disks, narrow and tortuous arteries, moderate distention of veins, old hemorrhages and numerous white exudates. The Hinton reaction of the blood was positive. Lumbar puncture revealed nothing abnormal except a protein content of 59 mg. per hundred cubic centimeters of fluid.

The diagnosis was anxiety neurosis and malignant hypertension.

CASE 28.—F. W., a 28 year old housewife, native-born, white, married, complained of night terrors, palpitation, fears and frigidity, of varied duration. She had had phobias as long as she could remember. Since her marriage, one and one-half years ago, she had had marked palpitation and shortness of breath. Two years ago routine urinalysis revealed sugar. There had been no recurrence of this. Physical examination revealed essentially a normal condition except for hyperactive deep reflexes. A barium sulfate enema and the gastrointestinal series of roentgenograms showed essentially a normal condition.

The diagnosis was anxiety neurosis and phobia.

CASE 29.—G. J., a 27 year old housewife, married, native-born, complained of asthma and overbreathing, of four weeks' duration. The patient had had attacks of asthma since the age of 31 and was sensitive to dust and various food products. During the past six weeks the attacks had increased markedly. She had had two hundred hypodermic injections during this time. She was awakened at night four weeks ago with marked hyperventilation and tetany. She stated that emotional situations often precipitated attacks of hyperventilation.

The diagnosis was bronchial asthma and hysteria.

CASE 30.—M. F., a 37 year old housewife, native, white, complained of abdominal pain, "feeling life" and worry about being pregnant, despite the fact that she was sterilized four years before. She felt tired, listless and blue, complained of crying spells, poor appetite and lack of sleep and did not do her housework well. Physical examination gave essentially normal results, except for obesity.

The diagnosis was: hypochondriasis, reactive depression and (?) involutional melancholia.

CASE 31.—M. T., 31 year. old nurse, white, married, native-born, complained of diarrhea, listlessness, irritability and insomnia. Fatigability had recently been marked, more so after an operation on the right tube. At times she complained of headaches and abdominal cramps. Physical examination, including taking an electrocardiogram, gave essentially normal results.

The diagnosis was reactive depression and hypochondriasis (?).

CASE 32.—A. C., a 44 year old man, white, unmarried, complained of "stomach trouble" for the last four years. He also stated that during this time he had had mild frontal headaches and aching in his arms and legs. He had had many examinations of the gastrointestinal tract, reported to show a normal condition. He believed, nevertheless, that there was "something the matter." He also complained that something was wrong in his chest—"no pain, but a feeling that it was empty at times." He wondered if he had cancer of the stomach or disease of the thyroid. Physical and neurologic examinations gave normal results. The basal metabolic rate was + 14 per cent.

The diagnosis was hypochondriasis and compulsion neurosis.

CASE 33.—C. M., a 16 year old girl, white, single, native-born, complained of attacks of weakness, dizziness and trembling, of eighteen months' duration. She also felt listless and indifferent. On further study, her indifference to her complaints and inability to get into relationship with the physician here was striking. She spoke little and remembered little about her past. Physical examination showed a systolic murmur at the apex of the heart. The result of the dextrose tolerance test was normal. Roentgenograms of the skull showed generalized prominence of the convolutional markings and those of the mastoids, sclerosis on both sides, more marked on the left. The intelligence quotient was 100.

The diagnosis was schizophrenia (?) and psychoneurosis, of mixed type.

CASE 34.—A. A., a 15 year old schoolgirl, white, single, native-born, complained of depression, tightness of the throat, frontal headache, feelings that her arms and legs were odd and did not belong to her and pressure in the head, of six months' duration. Physical examination revealed nothing abnormal.

The diagnosis was reactive depression and hypochondriasis.

CASE 35.—B. Q., a 31 year old housewife, white, married, native-born, complained of diarrhea, of seven months' duration. The symptom was immediately

preceded by the birth of her fifth child. In addition, she complained of lack of feeling of well-being, fatigability, uneasiness in her chest and vague, dull pains in her abdomen. She felt that her organs were falling down. She was somewhat depressed, but not suicidal. In personality she was precise, and had difficulty in deciding on any plan or course of action. Roentgenograms of the sinuses showed slight thickening of the mucous membrane of both antrums. A barium sulfate enema revealed nothing significant. The rest of the physical examination gave essentially normal results.

The diagnosis was hypochondriasis, with depressive factors.

CASE 36.—A. S., a 27 year old woman, single, Irish-American, complained of loss of appetite, belching of gas, occipital headaches and increasing irritability. At the age of 17 she had a pulmonary abscess, resulting in empyema and necessitating rib resection. The patient was rather self centered, aggressive and chronically depressed. Physical examination showed soft, blowing systolic murmurs at the apex and base of the heart and reversed tendon reflexes; gastric analysis and a barium sulfate enema revealed nothing abnormal.

The diagnosis was reactive depression and (?) hypochondriasis.

CASE 37.—P. S., a 27 year old Italian woman, married, a Catholic, complained of feelings of depression, lack of appetite and fleeting ideas of suicide. These feelings lasted a few days and then eased. She had similar feelings one day before the onset of her menses. Being a Catholic, she was concerned with the problem of contraception. One year ago she had an ulcer of the right leg. The present physical examination showed slight dulness in the lower right side of the chest and evidence of thickening of the pleura. The basal metabolic rates were —12 and —17 per cent. The sugar tolerance curve was within normal limits. The sodium content of the blood was 140 mg. The blood pressure was 105 systolic and 70 diastolic. Roentgenograms of the skull were normal.

The diagnosis was reactive depression and old abscess of the lung.

CASE 38.—H. W., a 33 year old salesman, married, white, native-born, complained of headache, abdominal pain, which was not localized, heart burn, tremor, dizziness and pressure in the head, of five years' duration. The onset occurred seven months after the patient's witnessing an automobile accident, in which a woman was killed. On questioning, he complained of a feeling that something was wrong in every system. Neurologic examination showed that the right pupil was larger than the left, ocular movements were poor and the deep reflexes were somewhat greater on the right than on the left. Lumbar puncture and encephalographic examination revealed nothing abnormal. The basal metabolic rates were —17, —9 and —6 per cent.

The diagnosis was hypochondriasis and (?) multiple sclerosis.

CASE 39.—V. R., a 24 year old woman, white, native, single, complained of fatigability, headaches and vague pains in her abdomen. At times she noticed aches and pains in her chest and in the muscles of her arms and had a feeling of not being up to par. She had also noticed twitchings in her arms since childhood. When the patient had difficult situations to contend with her symptoms became more marked. Physical examination and laboratory studies revealed nothing abnormal.

The diagnosis was hypochondriasis and (?) chronic encephalitis.

CASE 40.—T. F., a 51 year old man, divorced, white, native-born, complained of constipation, asthma, tinnitus, hand washing compulsion, headache, pain in the

stomach and flatulence, of eight years' duration. Physical examination showed removal of the right testicle, slight tenderness of the abdomen on palpation, hyperactive deep reflexes, hippus and bilateral tinnitus.

The diagnosis was compulsion neurosis and hypochondriasis.

CASE 41.—A. S., a 30 year old white man, native, single, complained of burning on urination and "urethal" discharge, of six years' duration. There were numerous other complaints, including headaches, feeling of tension at the top of the head, nosebleeds and tightness and the feeling of a lump in his throat. For the last six years he had had thumping of the heart and some discomfort in the cardiac region; he felt that his heart was going to stop and had difficulty in catching his breath. He had consulted a physician about "sour stomach." Examination showed that the stomach had sagged into the pelvis. He had pain in the arms, legs and hands. In addition, he felt "rotten" all over and had numbness in the arms and legs. During the past four years he had seen over thirty physicians, had spent $1,000 on them and had $100 worth of medicine at home. Physical examination revealed nothing abnormal.

The diagnosis was hypochondriasis.

Prof. Carl R. Doering, statistician of the Harvard University School of Public Health, cooperated in this study.

PROTECTIVE EFFECT OF CHOLESTEROL IN EXPERIMENTAL EPILEPSY

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Attention has turned in recent years to an explanation of the cause of epilepsy in terms of biochemical and physiologic dysfunction.[1] An excellent review of the research along these lines is provided in the monograph on epilepsy by Lennox and Cobb.[2]

The facts that fasting and a high fat, low carbohydrate diet are known to benefit patients with epilepsy [3] and that these procedures bring about changes in the concentration of blood lipids [4] have led to an investigation of the vital lipids in epilepsy.

Cholesterol, especially, has been studied. De Crinis [5] and Targowla, Badonnel and Berman [6] reported hypercholesteremia in patients with

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1. Kussmaul, A., and Tenner, A.: On the Nature and Origin of Epileptiform Convulsions Caused by Profuse Bleeding, and Also of Those of True Epilepsy, translated by E. Bronner, London, New Sydenham Society, 1859. Gowers, W. R.: Epilepsy and Other Convulsive Diseases: Their Causes, Symptoms and Treatment, London, J. & A. Churchill, 1881. Wilson, S. A. K.; Muskens, L. J. J.; Holmes, G., and Brain, W. R.: The Epilepsies, Brit. M. J. **2**:259-262, 1929.

2. Lennox, W. G., and Cobb, S.: Epilepsy from the Standpoint of Physiology and Treatment, Medicine **7**:105-290, 1928; Epilepsy, Harvard Medicine Monograph, Baltimore, Williams & Wilkins Company, 1928, vol. 14.

3. (*a*) Guelpa, G., and Marie, A.: La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire, Rev. de thérap. méd.-chir. **78**:8-13, 1911. (*b*) Geyelin, H. R.: Fasting as a Method for Treating Epilepsy, M. Rec. **99**:1037-1039, 1921. (*c*) Peterman, M. G.: The Ketogenic Diet in the Treatment of Epilepsy, M. Clin. North America **8**:1351-1352, 1925. (*d*) Lennox, W. G.: Ketogenic Diet in the Treatment of Epilepsy, New England J. Med. **199**:74-75, 1928. (*e*) Lennox, W. G., and Cobb, S.: Studies in Epilepsy: Clinical Effect of Fasting, Arch. Neurol. & Psychiat. **20**:771-779 (Oct.) 1928.

4. Shope, R. E.: Sugar and Cholesterol in Blood Serum as Related to Fasting, J. Biol. Chem. **75**:101-113, 1927. Bloor, W. R.: Diet and Blood Lipids, ibid. **95**: 633-644, 1932.

5. de Crinis, M.: Die Beteiligung der humoralen Lebensvorgänge des menschlichen Organismus am epileptischen Anfall, in Foerster, O., and Wilmanns, K.: Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1920, no. 22.

6. Targowla, R.; Badonnel, M., and Berman, A.: Sur la cholestérinémie dans les maladies mentales, Encéphale **18**:138-140, 1923.

epilepsy. Albertoni and Borgatti [7] also found hypercholesteremia in dogs during and after the induction of convulsions by the use of 20 per cent camphor in oil and direct electrical stimulation of the rolandic area. They concluded that the rise in cholesterol is secondary to disintegration of brain tissue rather than to any specific pathologic state. Pighini [8] found cholesterol in the cerebrospinal fluid of epileptic persons, which he attributed to cortical destruction since he found no cholesterol in the cerebrospinal fluid of normal persons. Goebel [9] found an increase in cholesterol in the cerebrospinal fluid of epileptic persons just before seizures. On the other hand, Pezzali,[10] Popea and Vicol [11] and Gray and McGee [12] noted hypocholesteremia. Osnato, Killian, Garcia and Mattice; [13] Duncan,[14] and Rosen, Krasnow and Notkin [15] reported essentially normal cholesterol levels in epilepsy.

Robinson, Brain and Kay [16] reported that hypocholesteremia was associated with epilepsy and, in 10 of 11 patients tested repeatedly both before and after convulsions, found that the blood cholesterol diminished before attacks and that the attacks occurred at about the lowest levels. A preparoxysmal fall in blood cholesterol was reported more recently by Gosden, Fox and Brain; [17] by Goodall,[18] and by McLean.[19]

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7. Albertoni, P., and Borgatti, G.: La colesterina del sangue e l'accesso epilettico, Policlinico (sez. med.) **38**:293-298, 1931.

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11. Popea, A., and Vicol, A.: Les variations de la cholestérinémie durant l'accès épileptique, Compt. rend. Soc. de biol. **93**:749-750, 1925.

12. Gray, H., and McGee, L. C.: Cholesterol Content of Blood in Epilepsy and in Feeblemindedness, Arch. Neurol. & Psychiat. **28**:357-369 (Aug.) 1932.

13. Osnato, M.; Killian, J. A.; Garcia, T., and Mattice, M. R.: Comparative Chemical Studies of Blood and Spinal Fluid in Epilepsy, Brain **50**:581-600, 1927.

14. Duncan, A. G.: Serum Cholesterol in Mental Disorders, J. Ment. Sc. **76**: 284-291, 1930.

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16. Robinson, S. H. G.; Brain, W. R., and Kay, H. D.: Association of Low Blood Cholesterol with Occurrence of Fits in Epileptics, Lancet **2**:325-326, 1927.

17. Gosden, M.; Fox, J. T., and Brain, W. R.: Cholesterol of Blood Plasma in Epilepsy, Lancet **2**:12-16, 1929.

18. Goodall, E.: Blood Cholesterol During Menstrual and Epileptic Cycles, Lancet **1**:384-386, 1929.

19. McLean, J. H.: Blood Cholesterol in Epilepsy in Relation to Treatment by Dehydration and Ketogenesis, J. Ment. Sc. **80**:82-86, 1934.

The studies on lecithin have been fewer. Bornstein [20] reported that there was an increased concentration of lecithin in the blood in epilepsy, as well as in various other nervous disorders. Feigl [21] reexamined Bornstein's data and concluded that the increase in lecithin was not a common phenomenon, but that when it did occur it was accompanied by other alterations in the blood lipids.

McQuarrie, Bloor, Husted and Patterson [22] reported on their studies of the blood lipids in epilepsy. The levels of lecithin, cholesterol and total fatty acids in the blood plasma were determined under various conditions for epileptic persons, as well as for a control group of nonepileptic subjects. No significant difference was found in the cholesterol values for the two groups, but in the epileptic group lecithin was found to be significantly lower and the total fatty acids to be significantly higher than in the nonepileptic group. The phospholipids and total fatty acids also showed a greater variability in epileptic than in normal persons. Repeated tests throughout the day of seizures showed no constant relationship between any one constituent of the plasma and the attacks. These investigators, however, noted a tendency for the ratio between lecithin and cholesterol to be higher at or near the time of attacks. They found that strongly ketogenic diets which benefited the epilepsy produced hypercholesteremia and hyperlecithinemia, but that attacks occasionally occurred in spite of the elevation in plasma lipids. The patient with the most severe epilepsy whom they studied had hypocholesteremia as a rule, and with attacks there was a marked increase in plasma lecithin without a significant change in plasma cholesterol. These authors tended therefore to stress the relation between the lecithin-cholesterol ratio and the attacks, rather than to attribute the seizures to alterations in any one plasma lipid that they studied. Recently, Cowie and Magee [23] studied various tissues of persons in status epilepticus for lipid content and found the ratio of lecithin to cholesterol to be much

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21. Feigl, J.: Ueber das Vorkommen und die Verteilung von Fetten und Lipoiden im Blute bei Geisteskrankheiten: Chemische Beiträge zur Kenntnis spezifischer Lipämien, Biochem. Ztschr. **88**:53-84, 1918.

22. (*a*) McQuarrie, I.; Bloor, W. R.; Husted, C., and Patterson, H. A.: Lipids of Blood Plasma in Epilepsy: Statistical Study of Single Determinations in One Hundred Epileptic and Thirty-Two "Normal" Subjects, J. Clin. Investigation **12**:247-254, 1933. (*b*) McQuarrie, I.; Husted, C., and Bloor, W. R.: Lipids of Blood Plasma in Epilepsy: Variations of Lipids in Relation to Occurrence of Seizures, ibid. **12**:255-265, 1933.

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higher than that for nonepileptic persons. This is in agreement with the findings of McQuarrie, Bloor, Husted and Patterson.[22a]

The wide distribution of cholesterol and lecithin throughout the vegetable and animal kingdoms attests their fundamental importance. It has been demonstrated [24] that these and certain fats, unlike the storage fats associated with adiposity, are qualitatively and quantitatively as constant in their presence as the proteins, and that this relationship is maintained even in the presence of the severe depletion of starvation. Recent research [25] has indicated that cholesterol and lecithin are essential elements of the cell membranes and, in fact, are of fundamental importance in determining the semipermeable characteristics of the cell membrane. The role they play in cell structure and metabolism is thus of the utmost importance. While cholesterol is thought to diminish the permeability of the cell membrane, lecithin is credited with the opposite effect, and a delicate balance between these two oppositely acting lipids is considered to be vital to normal cell function. This antagonism is further brought out by the hemolytic effect of lecithin as opposed to the antihemolytic effect of cholesterol [26] and the narcotic effect of cholesterol as opposed to the antinarcotic effect of lecithin.[27] This antagonism seems further borne out in the ionic attractions of the two agents. While lecithin attracts potassium through membranes,[26f] cholesterol retards its diffusion. Potassium increases the hygroscopic action of lecithin, while cholesterol and calcium retard it.[24] Also, the combination of cholesterol

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24. Leathers, J. B.: Role of Fats in Vital Phenomenon, Lancet **1**:803-807, 853-856, 957-962 and 1019-1022, 1925.

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26. (*a*) Bloor, W. R.: The Distribution of the Lipoids (Fat) in Human Blood, J. Biol. Chem. **25**:577-579, 1916; (*b*) Blood Phosphates in the Lipemia Produced by Acute Experimental Anemia in Rabbits, ibid. **46**:171-187, 1920. (*c*) Brinkman, R.: Experimental Anemia by Lecithine Injections, Nederl. tijdschr. v. geneesk. (pt. 1) **66**:2462, 1922. (*d*) Myers, V. C.: Chemical Changes in Blood and Their Clinical Significance, Physiol. Rev. **4**:274-328, 1924. (*e*) Muller, G. L.: Relation of Cholesterol, Lecithin Phosphorus and Fatty Acids to Remission of Pernicious Anemia, Am. J. M. Sc. **179**:316-337, 1930. (*f*) Shaw, B. H., and Sharpe, J. S.: Significance of Cholesterol in Cellular Oxidation and Its Bearing on Mental Disorder, J. Ment. Sc. **77**:53-66, 1931.

27. (*a*) Cashin, M. F., and Moravek, V.: Physiological Action of Cholesterol, Am. J. Physiol. **82**:294-298, 1927. (*b*) McQuarrie, Husted and Bloor.[22b]

and calcium in high concentration has been shown to produce cellular dehydration and shrinkage. These relationships are probably basic in character and, as expressed in the semipermeability of cell membranes, profoundly influence such fundamental functions as water metabolism,[28] acid-base equilibriums,[29] excitation and conduction in protoplasm [30] and cellular oxidation.[31]

Whether an abnormality in cholesterol or lecithin or in the simple ratio between these lipids is an etiologic factor in epilepsy is impossible to say with present knowledge. It is possible that some other factor is the direct cause and that the abnormality of the lipids is merely an associated phenomenon. Or, again, it is conceivable that many factors may disturb the metabolism and relationships of these lipids, which, in turn, may result in the final necessary conditions for production of the convulsive state. The multiplicity of factors which influence epilepsy, as well as the intricate interplay of biochemical substances known to be intimately associated with the delicate equilibriums of cellular physiology, suggests the latter concept as the more likely. This may be seen, for instance, in the relation between fatigue, epilepsy and exercise and the cholesterol content of the blood [16] (see "Comment," page 318).

That epilepsy may be intimately concerned with the lecithin-cholesterol balance is suggested by the following observations: 1. The increased incidence of convulsive seizures when the relative concentration of cholesterol is known to be diminished and, as the corollary, the

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29. (*a*) Bugnard, L.: Variations de la cholestérine, de la viscosité et du p_H du sang après la splénectomie, Compt. rend. Soc. de biol. **101**:546-548, 1929. (*b*) Sorkin, E., and Batuschanskaja, M.: Alimentäre Cholesterinämie und Blutzucker bei Diabetes, Ztschr. f. d. ges. exper. Med. **74**:138-147, 1930. (*c*) McQuarrie, Husted and Bloor.[22b] (*d*) Muller.[26e] (*e*) Cashin and Moravek.[27a] (*f*) Degkwitz.[28a] (*g*) Calvin and Goldberg.[28e]

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31. Muller.[26e] Shaw and Sharpe.[26f] Calvin and Goldberg.[28e]

diminished incidence of attacks with relatively higher levels of cholesterol. This is suggested by the variations in attacks with age,[32] season,[33] time of day,[34] stage of the menstrual cycle,[35] pregnancy,[36] state of alkalosis or acidosis,[29] hydration-dehydration balance [28] and such pathologic conditions as anemia, cachexia, prostration,[37] pneumonia,[38] schizophrenia,[39] cancer [40] and diabetes.[41]

2. Evidence that hypocholesteremia or a high lecithin-cholesterol ratio precedes and accompanies attacks of epilepsy.[42]

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32. Gordon, M. B., and Cohn, D. J.: Cholesterol and Lipoid Phosphorus in Infancy and in Childhood: Normal Incidence in Cord Blood and During Infancy and Early Childhood, Am. J. Dis. Child. **35**:193-200 (Feb.) 1928. Butter, A. J. M.: Age Incidence in Epilepsy, Brit. M. J. **2**:714-715, 1936.

33. Currie, A. N.: Cholesterol of Blood in Malignant Disease, Brit. J. Exper. Path. **5**:293-299, 1924.

34. Hopkins, H.: Time of Appearance of Epileptic Seizures in Relation to Age, Duration and Type of Syndrome, J. Nerv. & Ment. Dis. **77**:153-162, 1933; Chemical Studies in Epileptic Syndrome: Whole Blood Cholesterol, ibid. **77**:601-616, 1933; Chemical Studies in Epileptic Syndrome: Nocturnal and Diurnal Rhythm, Am. J. Psychiat. **92**:75-88, 1935.

35. Okey, R., and Boyden, R. E.: Studies of Metabolism of Woman: Variations in Lipid Content of Blood in Relation to Menstrual Cycle, J. Biol. Chem. **72**:261-281, 1927. Maddox, K.: Note on Diagnosis of Blood Cholesterol Changes in Major Convulsive Epilepsy, M. J. Australia **1**:531-534, 1931. Goodall.[18]

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39. Murphy, J. P. H.: Comparative Study of Epilepsy and Schizophrenia, M. J. & Rec. **128**:77 and 110, 1928. Alford, L. B.: Epilepsy and Dementia Praecox Considered as Types of Abiotrophy, J. Nerv. & Ment. Dis. **68**:594-601, 1928.

40. Volland: Ueber die Häufigkeit des Carcinoms bei Epilepsie, Ztschr. f. Krebsforsch. **28**:15-27, 1928. Hodskins, M. B., and Guthrie, R. H.: Cancer Complicating and Modifying the Course of Epilepsy: Review of Fifty-Five Cases, Am. J. Psychiat. **12**:877-892, 1933.

41. (*a*) Barborka, C. J.: Epilepsy in Adults: Results of Treatment by Ketogenic Diet in One Hundred Cases, Arch. Neurol. & Psychiat. **23**:904-914 (May) 1930. (*b*) Sorkin and Batuschanskaja.[29b] (*c*) Denis.[36a] (*d*) Bloor and Knudson.[36b]

42. Robinson, Brain and Kay.[16] Gosden, Fox and Brain.[17] Goodall.[18] McLean.[19] Bornstein.[20] Feigl.[21] McQuarrie, Bloor, Husted and Patterson.[22a] McQuarrie, Husted and Bloor.[22b] Cowie and Magee.[23]

3. The beneficial effects of ketogenic diets [43] and dehydration,[44] which have been shown to be associated with an increase in the cholesterol levels of the blood.[19] Similarly, sedatives and narcotics,[45] at least in part, may be of benefit because of the relative hypercholesteremia they produce. The beneficial results reported to be obtained with the injection of brain and nerve substance [46] may likewise arise from their relatively high cholesterol content.[23]

So much indirect evidence seemed worthy of further study.

METHOD

As a direct approach to this problem, it was decided to study the effect of intravenous and parenteral injections of cholesterol on the convulsive threshold of animals in which experimental epilepsy was induced with carefully controlled and complete analyses of the blood and tissue lipids. Such a direct alteration of the tissue cholesterol, with correlated studies on the blood and tissue lipids and the effect on experimental epilepsy, might well adduce valuable evidence concerning the part the lipids play in epilepsy.

The present study represents the initial attack on the problem of epilepsy from this point of view. Preliminary tests showed that variations from animal to animal and from one time to another were too great for satisfactory tests on the individual animal. Consequently, the statistical method proved necessary, and white mice were selected for the study. Injections of cholesterol were made by the intraperitoneal route. Biochemical studies on the tissue lipids were carried out on both control and test groups of mice and will be the subject of a separate report.

Although cholesterol has been injected numerous times in the experimental study of arteriosclerosis [47] and cholesterol metabolism,[48] its successful injection

43. Peterman.[3c] Lennox.[3d] Gray and McGee.[12] McLean.[19] McQuarrie, Husted and Bloor.[22b] Barborka.[41a]

44. McLean.[19] Shaw and Sharpe.[26f] Degkwitz.[28a]

45. McQuarrie, Husted and Bloor.[22b] Cashin and Moravek.[27a]

46. Choroschko, W. K.: Versuch einer biochemischen therapeutischen Einwirkung bei Epilepsie (Einverleibung von Nervengewebe, Blutgerinnung): Vorläufige Mitteilung, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:545-551, 1925. Nóvoa Santos, R.: Tratamiento de la epilepsia mediante inyecciones de emulsión de substancia cerebral en una solución de luminal sódico, Arch. de neurobiol. **7**:213-217, 1927; Arch. de med., cir. y especialid. **27**:393, 1927. Lombardi, A.: L'opoterapia cerebrale nella cura dei malarici epilettici, Rev. sud.-am. de endocrinol. **2**:388-392, 1928. Stawrowskaja, M. N.: Ueber die Ergebnisse der Behandlung der Epilepsie mit Gehirnemulsion, Monatschr. f. Psychiat. u. Neurol. **74**:221-233, 1929. Kimball, O. P., and Gudakunst, D. W.: Study of Epilepsy in Detroit: Preliminary Report (on Treatment with Lipoids of Brain Tissue), J. Michigan M. Soc. **35**:641-644, 1936.

47. Scarff, R.: Production of Experimental Atheroma with Cholesterol, J. Path. & Bact. **30**:647-665, 1927. Rosenthal, S. R.: Studies in Atherosclerosis:

(Footnotes continued on next page)

offers considerable difficulty because of its insolubility in water. The following agents were tested as vehicles for cholesterol: acacia, olive oil, ethylene glycol, diethylene glycol, ethyl diethylene glycol, butyl diethylene glycol, three "glyco" solvents, benzyl benzoate, ethyl citrate, ethyl carbonate, ethyl lactate, ethyl malonate, ethyl maleate, ethyl cinnamate, ethyl butyrate, ethyl n-caproate, ethyl fumarate, ethylene glycol dibutyrate and ethylene glycollate.

Although relatively high concentrations of cholesterol were soluble in ethyl cinnamate, ethyl n-caproate and ethyl butyrate, toxicity tests on white mice demonstrated their impracticability. A 3 per cent solution of cholesterol in olive oil was found to be safe and practical. Also, a 3 per cent suspension of cholesterol in water, obtained by repeated passage through a colloid mill, was found to be fairly satisfactory and entirely safe. These 3 per cent preparations were finally selected and proved adequate for the purposes of this study. Crystalline cholesterol, chemically pure,[49] pure olive oil and distilled water were used for the injections.

The mice were kept under standard conditions, on a diet of dog chow pellets (purina). Injections of 0.1 cc. of a 3 per cent solution of cholesterol in olive oil were given every other day for twelve days. The same number of injections of 0.1 cc. of plain olive oil, given under corresponding conditions, was used as a control. Other experiments employing fewer injections, at different intervals and of varying doses, were performed to determine the dosage and conditions necessary to obtain a protective effect with cholesterol.

A few experiments involving the trial of a 3 per cent colloidal suspension of cholesterol in water were made. In this series, six injections of 0.1 cc. of the suspension were given every other day. Injections of distilled water were made as controls.

Various convulsive agents were tried, and cocaine hydrochloride was finally selected for this study. Its effect on mammals has been shown to be primarily cortical.[50] Although animals are presumed not to acquire tolerance to cocaine,[51] exhaustive preliminary studies showed conclusively that white mice become tolerant to a considerable degree. Repeated injections of graded doses were tolerated. Although the dose was increased by two thirds, the incidence of convulsions and death remained approximately the same. For this reason tests were

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Chemical, Experimental and Morphologic; Roles of Cholesterol Metabolism, Blood Pressure and Structure of Aorta; Fat Angle of Aorta (F. A. A.), and Infiltration-Expression Theory of Lipoid Deposit, Arch. Path. **18**:473 (Oct.); 660 (Nov.) 1934. Page, I. H., and Bernhard, W. G.: Cholesterol-Induced Atherosclerosis: Its Prevention in Rabbits by Feeding of Organic Iodine Compound, ibid. **19**:530-536 (April) 1935. Duff, G. L.: Experimental Cholesterol Arteriosclerosis and Its Relationship to Human Arteriosclerosis, ibid. **20**:81 (July); 259 (Aug.) 1935. Downs, W. G., Jr.: Lecithin in Experimental Arteriosclerosis: Preliminary Study, Am. Med. **41**:460, 1935.

48. Chamberlain, E. N.: Cholesterol Content of Normal Tissues and Effect of Intravenous Injections of Cholesterol Thereon, J. Physiol. **66**:249-261, 1928.

49. Cholesterol was obtained from the Wilson Laboratories, Chicago.

50. Feinberg, I.: Weitere Mittheilungen zur physiologischen Cocainwirkung, Berl. klin. Wchnschr. **24**:166-168, 1887. Morita, S.: Untersuchungen an grosshirnlösen Kaninchen: I. Das Verhalten der Blutzuckerkonzentration, Arch. f. exper. Path. u. Pharmakol. **78**:188-207, 1915.

51. Grode, J.: Ueber die Wirking längerer Cocaindarreichung bei Tieren, Arch. f. exper. Path. u. Pharmakol. **67**:172-190, 1911-1912.

strictly limited. In the results reported the mice were exposed to cocaine only once. A 6 per cent solution of cocaine hydrochloride, injected subcutaneously in the back, proved most satisfactory and was used throughout the study.

Various doses of cocaine hydrochloride were tried on control groups of white mice. A dose of 96 mg. per kilogram of body weight was finally adopted as the standard, since it gave the greatest spread of effects. This dose and the resultant wide spread of effects were important factors from the standpoint of the comparative results essential in this study. In other words, the dose which produced no effect, petit mal, grand mal or death in varying proportions among the mice proved more satisfactory for demonstrating variations of the protective effect than larger doses, which resulted in a higher percentage of deaths, or smaller doses, which resulted only in slight involvement.

Consistent results were found to be dependent largely on the accuracy of weighing the mice and of injecting the exact calculated dose. A triple beam balance, accurate to 0.01 Gm., proved adequate for weighing the mice, while a specially calibrated precision attachment, used in conjunction with a tuberculin syringe, assured injection of doses accurate to 0.002 cc.

For the convulsive tests, the following criteria were adopted to distinguish the various phases and stages of reaction:

1. *Nonconvulsive Reaction.*—This stage was usually characterized by a considerable degree of hyperactivity or depression. Various degrees of ataxia were frequently noted, as well as a tendency to weakness in the hindlegs.

2. *Convulsive Reaction.*—(*a*) Petit Mal: Falling or stumbling, when apparently due to a momentary lapse of consciousness, occurred sometimes only once or twice in the course of the observation but usually repeatedly, and occasionally persisted over long periods without progressing into grand mal seizures. The tail tended to become stiff and straight, and slight frothing at the mouth was frequently observed. (*b*) Grand Mal: (1) Tonic phase: This consisted of a predominating extensor spasm with loss of consciousness for at least several seconds; opisthotonos frequently occurred, with the tail twisting back over the body; frothing at the mouth was uniformly observed. (2) Clonic phase: This occurred far more frequently than the simple tonic spasm and consisted of clonic movements of the legs and body. Sometimes clonic movements of the forelegs alone occurred, in conjunction with opisthotonos and loss of consciousness, but usually the convulsions were generalized and violent. The grand mal seizures lasted from several seconds to several minutes, and repeated seizures often occurred over a period of an hour. Frothing at the mouth was marked. The same animal frequently shifted from one convulsive stage to another, the order of change almost always being progressive from the lighter to the more severe type.

3. *Death.*—Cases of immediate death from accidental intravenous injections were not included.

Time was carefully recorded from the moment when the cocaine was injected and proved of value in distinguishing the reactions following the injections of cholesterol, oil and water. No effort was made to drive the mice into convulsions, since such stimulation only introduced a variable and uncontrollable factor.

Follow-up observations were made from the time of injection till one and a half hours or more after the last observed effect. The results were recorded from individual observations on each mouse and indicate the most severe stage attained by each. Spots of coloring on the back served to distinguish and identify the mice.

RESULTS

The detailed results of this study are presented in table 1. The protective effect of direct, parenteral injections of cholesterol was definite. The protective effect observed with the solution of cholesterol in olive oil was pronounced, while that of the colloidal cholesterol was

TABLE 1.—*Protection of Cholesterol Against the Convulsive Effects of Cocaine Hydrochloride in White Mice*

Substance Injected	Dose	No. of Injections (q.2 d.)	No. of Mice	Interval Between Injections and Test, Days	Dose of 6% Cocaine Hydrochloride, Mg./Kg.	Results of Tests: No Convulsions	Petit Mal	Grand Mal	Fits and Death	Involvement, %
Olive oil (control), cc.	0.1 cc.	6	29	3	120	0	3	4	22	100
	0.1 cc.	6	30	1	120	1	1	8	20	97
	0.1 cc.	6	28	2	102	2	4	6	16	93
	0.1 cc.	6	27	2	90	13	2	6	6	52
	0.1 cc.	6	29	1	96	7	7	5	10	76
	0.1 cc.	6	29	2	96	8	3	6	12	73
	0.1 cc.	6	28	3	96	5	4	7	12	82
3% solution of cholesterol in olive oil	0.1 cc.	6	30	1	120	2	4	8	16	93
	0.1 cc.	6	60	2	120	13	10	7	30	78
	0.1 cc.	6	53	3	120	4	5	8	36	92
	0.1 cc.	6	30	6	120	4	3	11	12	87
Duration of protective effect	0.1 cc.	6	27	1	96	7	2	7	11	74
	0.1 cc.	6	29	2	96	22	4	1	2	24
	0.1 cc.	6	30	3	96	19	5	2	4	37
	0.1 cc.	6	25	7	96	8	3	6	8	68
	0.1 cc.	3	28	2	96	22	3	0	3	22
	167 mg./Kg.	3	30	1	96	23	2	1	4	24
	167 mg./Kg.	3	28	2	96	24	0	4	0	14
	167 mg./Kg.	3	27	3	96	19	1	5	2	30
	167 mg./Kg.	3	30	4	96	19	3	6	2	37
Dose and number of injections	71 mg./Kg.	3	18	2	96	4	5	7	2	78
	100 mg./Kg.	3	29	2	96	18	1	5	5	38
	145 mg./Kg.	3	27	2	96	18	1	5	3	33
	200 mg./Kg.	3	27	2	96	15	4	4	4	45
	143 mg./Kg.	2	30	2	96	16	2	7	5	47
	0.1 cc.	1	28	2	96	11	2	9	6	61
	200 mg./Kg.	1	28	2	96	12	0	4	12	57
	167 mg./Kg.	3 (q.d.)	28	1	96	17	2	3	6	39
Water (control), cc.	0.1 cc.	6	30	2	96	13	4	4	9	57
	0.1 cc.	3	29	2	96	10	2	6	11	65
	0.1 cc.	3	28	3	96	8	4	12	4	72
3% suspension of cholesterol in water, cc.	0.1 cc.	6	29	1	120	5	2	9	13	83
	0.1 cc.	6	29	1	96	18	1	2	8	38
	0.1 cc.	6	28	2	96	16	5	3	4	43
	0.1 cc.	6	24	3	96	13	1	5	5	46

less striking. A series of three injections of the doses of cholesterol proved as satisfactory as six, but one or two injections afforded less satisfactory protection, even though very large doses of cholesterol were used. Variation of the dose of cholesterol in olive oil (administered in three injections) showed that protection varied roughly in proportion to the dose.

The duration of the protection of cholesterol proved to be an interesting phase of the study. Tests made shortly after the last injection

of cholesterol, even twenty-four hours later, showed less protection than on the second day after the final injection of cholesterol. With the same dose of cholesterol and the same number of injections, maximum protection was attained about the second day after the final injection of cholesterol. Other tests, on the third and fourth days after the final injection of cholesterol, showed the protective effect to be progressively diminishing, and after a week no definite protection could be shown. In an effort to throw further light on the apparent negative phase of protection in the period immediately following the last injection of cholesterol, a series of three injections of cholesterol were given on successive days, and the cocaine test was performed twenty-four hours later. An intermediate degree of protection resulted.

STATISTICAL ANALYSIS OF RESULTS [51a]

Statistical analysis of the results obtained for the control groups receiving injections of olive oil and tested with a dose of 96 mg. of cocaine hydrochloride per kilogram of body weight indicated that the variations observed were well within the range that might be expected on the basis of chance. With an X^2 (square contingency) of 0.59 and 2 degrees of freedom, the probability that the variations observed in these groups occurred purely by chance was 75 per cent. Thus, in spite of the fact that these groups were tested at different intervals following the last injection of olive oil, they may be considered as a single control group and compared as such with the groups given injections of cholesterol dissolved in olive oil.

A survey of the results obtained in the various test groups prepared by preliminary injections of cholesterol dissolved in olive oil suggested the comparableness of the three groups which received three or six injections of 167 mg. of cholesterol per kilogram of body weight, or the approximate equivalent of 0.1 cc., and which were tested on the second day following the last injection by 96 mg. of cocaine hydrochloride per kilogram. Analysis of these three groups by means of X^2 gave a value of 0.183. With 2 degrees of freedom the probability, therefore, was 91 per cent that the variations observed in these three test groups occurred merely by chance. Thus it may be concluded that, under the conditions of these tests, six preliminary injections of cholesterol had no more effect than three.

A comparison, by means of Yule's Q (coefficient of association),[52] of these three test groups and the control groups receiving olive oil alone is presented in table 2A. As is indicated, the results are highly significant and substantiate the conclusions previously stated.

In similar fashion, the two tests performed three days after the last injection of cholesterol appear, by statistical analysis, to be comparable. The X^2 of these groups was 0.105, and with 1 degree of freedom the probability was 75 per cent that the observed differences were purely due to chance. This might have been anticipated as a result of the previous analysis, since the only variations of

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51a. Dr. E. P. Lucia, assistant professor of biometry, department of hygiene, of the University of California, gave criticism and advice in connection with the statistical analysis of these results.

52. Yule, G. U., and Kendall, M. G.: An Introduction to Study of Statistics, ed. 11, London, Charles Griffin & Company, Ltd., 1937.

procedure—three instead of six preliminary injections of roughly equivalent doses (0.1 cc. and 167 mg. per kilogram) of cholesterol—had proved inconsequential in the previous analysis. Comparison of these two test groups with the control groups by means of Yule's Q (table 2 B) again shows that the protective effect of cholesterol is definite on the third, as well as on the second, day after the last injection of cholesterol.

Likewise, the variations in the results observed in the control groups which received injections of water were found to be insignificant. The X^2 for these groups was 0.86, and with 2 degrees of freedom the probability was 66 per cent that the observed variations occurred merely by chance and that the differences in the number of preparatory injections of water and the variations in the intervals between the last injection of water and the day of the test were of no significance. These groups, therefore, may also be allocated to a single group for the sake of comparison with those receiving the cholesterol suspended in water.

The X^2 of the three groups receiving the colloidal suspension of cholesterol in water and tested with 96 mg. of cocaine hydrochloride per kilogram was 0.158. With 2 degrees of freedom the probability was 92 per cent that the variations observed in these groups were due purely to chance. Thus, the suggestive correlation between the interval from the last injection of cholesterol to the day of the test and the percentage of convulsive involvement was not significant. These three test groups may be compared, therefore, as a unit with their control, the three groups receiving injections of water and tested with the same dose of cocaine hydrochloride. Comparison of these groups by means of Yule's Q is shown in table 2 C and mathematically substantiates the conclusions previously made with respect to the protective effect of cholesterol in an aqueous colloidal suspension.

A delayed onset of the effects of cocaine was observed in the test groups of mice receiving protective injections of cholesterol as compared with the onset of effects in the control groups. The details of this phenomenon are presented in table 2, and its significance is considered in the general comment (page 319).

COMMENT

Direct injection of cholesterol has been shown to have a sedative effect.[45] The question therefore arises as to whether the protection from cholesterol noted in this study may not be a direct result of sedation. The following observations have convinced us that this explanation is not valid. After the initial injection of cholesterol in olive oil the mice became quiet and tended to go to sleep. They could readily be aroused, however, which argued against any marked degree of sedation. Within two or three hours they had resumed their normal activities. After the second injection of cholesterol the same effect was noticed, but only to a minor degree. The sedative effect after the third injection of cholesterol was minimal or absent. Since the protective effect was not maximal directly after the injection of cholesterol, that is, during the period of possible sedation, and protection increased with later injections inversely as the sedative effect diminished, it is difficult to relate these two factors or to explain the protective phenomenon on the basis of a sedative effect.

It is by no means certain that (in accordance with the hypothesis stated in the beginning of this article) the protection provided by the cholesterol resulted from the metabolic utilization of the injected cholesterol to lower the permeability of cell membranes and consequently to reduce cortical irritability. One important fact, however, consistently observed in this study tends to be in accordance with this explanation. The onset of the effects following the injection of cocaine hydrochloride in the control groups of mice (given injections of water and olive oil) usually occurred within from one-half to three minutes.

TABLE 2.—*Statistical Analysis, by Means of Yule's Q, of the Protection Afforded by Cholesterol Against the Convulsive Effects of Cocaine Hydrochloride (96 mg. Per Kilogram) in White Mice, as Shown by Comparison with Control Groups Similarly Tested*

A. The control group received olive oil and the test group cholesterol dissolved in olive oil. The test was made on the second day following the final injection of cholesterol.

Group	No Convulsions	Convulsions	Total	
Test	68	17	85	
Control	20	66	86	$Q_Y = 0.859 \pm 0.048$*
Total	88	83	171	

B. The control group received olive oil and the test group cholesterol dissolved in olive oil. The test was made on the third day following the final injection of cholesterol.

Group	No Convulsions	Convulsions	Total	
Test	38	19	57	
Control	20	66	86	$Q_Y = 0.737 \pm 0.088$*
Total	58	85	143	

C. The control group received injections of water and the test group injections of a colloidal suspension of cholesterol in water.

Group	No Convulsions	Convulsions	Total	
Test	47	34	81	
Control	31	56	87	$Q_Y = 0.428 \pm 0.120$*
Total	78	90	168	

* Since a value three or more times that of the standard error may safely be considered a significant coefficient of association, the calculated values of Yule's Q clearly indicate that cholesterol protects against convulsions produced under the conditions of these experiments.

In the test groups receiving protective injections of cholesterol, the effects were definitely delayed, generally coming at from two to six minutes after the injection of cocaine hydrochloride, and often much later. Since the onset of effects was dependent on the cortical absorption of cocaine hydrochloride, this delay indicated slow absorption. In fact, the protective effect itself seems to be logically explained by the phenomenon of retarded absorption. With the dose of cocaine hydrochloride used in this study minor alterations in the rate of absorption might conceivably result in the variation of effects noted. In the presence of continual dispersion of the injected cocaine hydrochloride and loss by excretion, a delayed rate of cortical absorption would result in effective protection. Analysis of the data showing the relation between the degree of pro-

tection and the time of onset of the effects following the administration of cocaine hydrochloride is presented in table 3.

The results of this study, therefore, not only are consistent with the hypothesis that lowered permeability is an important factor in epilepsy but may be interpreted as suggestive evidence supporting that hypothesis.

On the basis of recent observations regarding the mode of action of convulsive drugs of the metrazol type,[53] we cannot escape the necessity of considering seriously intracellular anoxemia as a possible cause of convulsions in epileptic persons. Likewise, there is reason to believe that other fundamental physiologic mechanisms, such as hydration, alkalosis, and the accumulation of certain stimulatory drugs and metabolites, may operate on the cellular mechanism to produce convulsions. Alteration of any single factor undoubtedly affects many, if not all, other factors involved in the delicate equilibriums of cellular

TABLE 3.—*Protection Against Cocaine Hydrochloride (96 Mg. Per Kilogram of a 6 Per Cent Solution) and Time of Onset of Effects Following Its Administration*

Substance Injected	No. of Mice Tested	No. of Mice Affected	Protection, Percentage	Involvement with Respect to Time of Onset of Effects of Cocaine Hydrochloride, Percentage	
				0-5 Min.	5 Min. or More
Olive oil	113	82	23	76	24
Water	87	55	36	73	27
3% suspension of cholesterol in water	81	34	58	62	38
3% solution of cholesterol in olive oil	108	70	50 and less	64	36
	116	45	50-75	60	40
	115	24	75 and more	33	67

metabolism. Furthermore, such alterations with respect to the equilibrium between the cells and their environment would affect, and in turn be modified by, the semipermeable characteristics of the cell membranes. Thus, regardless of the exact etiologic relationships of the factors involved in the production of convulsions, cellular semipermeability should play a predominant role.

Semipermeability is a much abused term but, as properly used in the physicochemical sense, implies a selective specificity for the transmission or failure of transmission of metabolites and drugs in solution. Also, the terms anoxemia, hydration and alkalosis have a relative significance. Their importance for the cellular economy lies in the fact that the biochemical factors concerned with cellular metabolism, as well as the products of this metabolism, must be maintained within critical ranges of concentration, above or below which deviation from "normal"

53. Himwich, H. E.; Bowman, K. M.; Fazekas, J. F., and Orenstein, L. L.: Effect of Metrazol Convulsions on Brain Metabolism, Proc. Soc. Exper. Biol. & Med. **37**:359-361, 1937.

activity may take place. Since the physicochemical state of cells is dependent on a continuous, dynamic equilibrium between the cell and its surrounding medium, the overwhelming importance of semipermeability is inescapable. For example, the degree to which oxygen enters the cells is properly controlled by the status of the semipermeable membranes surrounding the cells. In other words, perhaps the most simple and direct approach to the etiologic factors in the convulsive state, from the physicochemical point of view, is to assume that it is brought about by interference, direct or indirect, with the permeability of the cell membrane. This does not necessarily imply that permeability is the final common mechanism for the production of the convulsive state. It is more probable that such a mechanism as cellular anoxemia is the final necessary condition for seizures and that the other mechanisms alter permeability of the cell membrane, which, in turn, acts to produce the necessary final mechanism (anoxemia or other condition). The intimate, reciprocal relationships between the functional state of the cell —hypoactivity or hyperactivity—and such fundamental states in cellular metabolism as hydration and dehydration, oxygenation and anoxemia, alkalosis and acidosis, and the obvious importance of permeability of the cell membrane in maintaining and regulating the delicate equilibriums of cellular metabolism, strongly suggest the mechanism of permeability as a common pathway for these various conditions in the production of the final, necessary state (anoxemia or other condition) preceding and leading to convulsions. The other possible explanation, that of multiple convulsive mechanisms (such as hydration, alkalosis and anoxemia, each acting directly on cellular metabolism to produce functional explosions), appears to be unlikely. In this sense, then, permeability of the cell membrane seems to be the logical physiologic common denominator of the convulsive picture.

As for cholesterol, its function may not be to produce a general decrease in the permeability of the cell membrane, for example, by lowering the level of water equilibrium within the cell. Its action may be to prevent the adsorption by the cell membrane of drugs or circulating metabolic products which tend to lower the permeability of the cell membrane to oxygen. Anoxemia, which causes an increase in intracellular metabolites and consequent hyperreactivity, would thus be avoided. Other possible theoretic mechanisms, of course, may explain the convulsive state in terms of cholesterol and permeability. The value of the concept of permeability in production of epilepsy lies in the fact that it takes into consideration an obviously important factor in cellular metabolism and one by which the various physiologic mechanisms known to favor the production of seizures may be correlated and better understood.

CONCLUSIONS

1. Direct parenteral injection of cholesterol in white mice resulted in a marked rise in the threshold for convulsive doses of cocaine hydrochloride. Both a colloidal suspension of cholesterol in water and a solution of cholesterol in olive oil showed this protective effect. The doses of cholesterol and the number of injections necessary to produce protection, as well as the duration of the effect, were determined experimentally.

2. After a series of protective injections of cholesterol in white mice, the convulsive effects of cocaine hydrochloride were more delayed in onset than the corresponding effects in control groups. This was interpreted as indicating delayed absorption of the convulsive agent. The protective effect, likewise, was explained on this basis. The results of this study were thus interpreted as consistent with the theory that the vital lipids play a significant role in the permeability of cell membranes and through this mechanism are an important factor in epilepsy.

Case Reports

AN UNUSUAL FORM OF LYMPHOCYTIC CHORIOMENINGITIS

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Lymphocytic meningitis was originally described as an acute, self-limited, benign inflammation of the meninges. However, since the original presentation of this condition as a primary clinical syndrome by Wallgren,[1] in 1925, several interesting case reports have appeared in the literature which indicate that this may not always be an innocuous disease.

The condition in Wallgren's cases was characterized by an acute onset, and the symptoms usually consisted of nausea, vomiting, slight elevation of temperature and evidences of meningeal irritation. The disease had a benign course, lasting about ten days. Recovery was complete, and there were no sequelae. Since the original account by Wallgren, the same syndrome has been described by numerous investigators. The clinical features of the illness have come to be well recognized, and, in addition, a virus has been isolated within the past few years which is considered to be the etiologic agent in at least one type of lymphocytic meningitis. Most of the work on this virus has been done by Armstrong [2] and Rivers [3] and their co-workers. Their investigations have shown that in some cases the virus can be demonstrated in the spinal fluid early in the course of the disease, while later virucidal antibodies appear in the blood. It has been suggested by Armstrong that the condition which is caused by the virus be given the designation of benign lymphocytic choriomeningitis, since it is possible to grow this virus in the chorio-allantoic membrane of the chick embryo.

As early as 1930, cases of lymphocytic meningitis were recorded in the Norwegian literature in which there were atypical features in the form of residual involvement of the central nervous system. Andersen and Wulff [4] studied 35 cases of lymphocytic meningitis which occurred in Copenhagen, Denmark, during the years 1917 to 1928 and in which the condition of the patients was checked by questionnaire in 1929. Of

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1. Wallgren, A.: Une nouvelle maladie infectieuse du système nerveux central? Acta pædiat. **4**:158-182, 1925.

2. (*a*) Armstrong, C., and Lillie, R. D.: Experimental Lymphocytic Choriomeningitis of Monkeys and Mice Produced by Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, Pub. Health Rep. **49**:1019-1027 (Aug. 31) 1934. (*b*) Armstrong, C., and Wooley, J. G.: Benign Lymphocytic Choriomeningitis, J. A. M. A. **109**:410-412 (Aug. 7) 1937.

3. Rivers, T. M., and Scott, T. F. M.: Meningitis in Man Caused by a Filterable Virus, Science **81**:439-440 (May 3) 1935.

4. Andersen, M. S., and Wulff, F.: Acute, Benign, Idiopathic, Serous Meningitis, Ugesk. f. læger **92**:572-575 (June 12) 1930.

these patients, 2 still had complaints of periodic headaches, and 1, of dizziness, forgetfulness and fainting spells; 2 had presented the symptoms and signs of chronic encephalitis. During the same year, Gunther [5] summarized the literature on lymphocytic meningitis, recording over 100 cases, 13 of which were his own. In 2 of the latter there were late manifestations consisting of changes in personality. Four cases of lymphocytic meningitis were reported from France by Roch,[6] in 2 of which there were residual manifestations. In 1 patient there was persistent diminution in the deep reflexes on the right side, while the other showed a masklike facies and absence of the winking reflex, suggesting the picture of a mild parkinsonian syndrome. Eckstein [7] reported an epidemic of lymphocytic meningitis, in which 13 persons were afflicted; 1 had strabismus as a permanent sequel of the disease.

The first reports in the American literature were published in 1929 by Viets and Watts; [8] in 1934 their third paper appeared, in which they described 14 cases. In 1 of these residual involvement of the central nervous system was manifested by headaches, fatigue, mental depression and impairment of memory.

Findlay, Alcock and Stern [9] reported 2 unusual cases of lymphocytic meningitis. In the first there developed complete paralysis of both lower extremities, and several months after the onset of the meningitic symptoms the patient still showed residual involvement of the lower extremities. The second patient also suffered weakness of both lower extremities, as well as bilateral paresis of the facial muscles; after recovery from the illness the right facial palsy persisted. From the cerebrospinal fluid of each patient these authors obtained a virus which proved to be identical with the virus isolated by Armstrong. Barker and Ford [10] studied a patient afflicted with lymphocytic meningitis in whose spinal fluid the virus of lymphocytic meningitis was found. During convalescence this patient experienced nausea, vomiting, difficulty in urination and a convulsive seizure. Within the next few months she manifested paresis of the lower extremities and sensory disturbances. Exploratory operation revealed severe chronic arachnoiditis obliterating a large portion of the spinal subarachnoid space. The result in this instance was spastic paraplegia, vesical dysfunction and a disturbance in sensation, both deep and superficial, below the distribution of the fourth thoracic segment.

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5. Gunther, A.: Ueber akute, „aseptische" Meningitis, Jahrb. f. Kinderh. **128**: 127-154 (July) 1930.

6. Roch, M.: Encore la méningite lymphocytaire bénigne: La forme méningée de l'encéphalite épidémique,, Rev. méd. de la Suisse Rom. **51**:1-18 (Jan. 15) 1931.

7. Eckstein, A.: Epidemische Meningitis serosa, Ztschr. f. Kinderh. **50**:564-595, 1931.

8. Viets, H. R., and Watts, J. W.: (*a*) Three Cases of Aseptic (Lymphocytic) Meningitis, New England J. Med. **200**:633-634 (March 28) 1929; (*b*) Acute Aseptic Meningitis, J. Nerv & Ment. Dis. **80**:253-273 (Sept.) 1934.

9. Findlay, G. M.; Alcock, N. S., and Stern, R. O.: The Virus Aetiology of One Form of Lymphocytic Meningitis, Lancet **1**:650-654 (March 21) 1936.

10. Barker, L. F., and Ford, F. R.: Chronic Arachnoiditis Obliterating the Spinal Subarachnoid Space, J. A. M. A. **109**:785-786 (Sept. 4) 1937.

Even more striking is the case reported by Viets and Warren [11] of a man aged 20 who succumbed to his illness two weeks after its onset. During the first part of the illness the patient had symptoms typical of lymphocytic meningitis. Except for photophobia, he seemed to be making a normal convalescence when, during the thirteenth day of his illness, he suddenly became restless, had convulsive seizures and died. Autopsy observations, the only ones reported thus far, included extensive meningoencephalitis involving all the brain tissue, but most marked in the region of the midbrain and pons. The microscopic changes consisted of perivascular lymphocytic infiltrations, glial nodules, petechial hemorrhages and large swollen ganglion cells, filled with inclusion bodies and pigmented granules. The ganglion cells of the cerebrum were only slightly affected, while those in the midbrain showed extensive changes with numerous cytoplasmic inclusion bodies, which were irregular and rod shaped. The spinal cord was also involved and presented mild perivascular infiltration and some gliosis. Unfortunately, the laboratory procedures necessary to demonstrate either a virus or virucidal antibodies could not be carried out. Consequently, it is not certain that this case was an example of the specific form of the malady in which the virus has been established as the causative agent. It does, however, represent the only reported case in which there were clinical manifestations of primary lymphocytic meningitis and a fatal outcome, and it suggests, furthermore, that occasionally the illness may become grave, in spite of an initial mild clinical course.

Hammes [12] reported 3 cases of lymphocytic meningitis, in 1 of which pleocytosis was still present five months after the onset of the illness. However, because this patient gave a history of syphilitic infection, the cause of the pleocytosis was somewhat doubtful. Another case was mentioned by this author in which a definite psychosis, associated with delusions and hallucinations, followed improvement from the meningitis; this patient recovered after four months.

In view of the generally accepted opinion that lymphocytic meningitis is a benign malady with a definite, self-limited course and complete clinical recovery, it seems advisable to add to the literature reports of cases in which unusual features were shown. It is for this reason that the following case is described.

REPORT OF A CASE

History.—S. L., a man aged 49, was admitted to the University Hospitals on July 16, 1937, with the principal complaint of frontal headache. The headache had been present for two weeks, during which it had increased in severity. Two days prior to admission stiffness of the neck appeared. The illness came on without premonitory symptoms; prior to its development the patient had always been in good health. He had had no previous nervous or mental ailment and gave no history of tuberculosis or syphilis. No other member of his family was ill, and there was no known exposure to infection. The patient was born and reared in

11. Viets, H. R., and Warren, S.: Acute Lymphocytic Meningitis, J. A. M. A. **108**:357-361 (Jan. 30) 1937.

12. Hammes, E. M.: Acute Lymphocytic Meningitis, Minnesota Med. **21**:151-154 (March) 1938.

Norway, having been in the United States only seven years. He had worked in a western state before settling on a small farm in Minnesota, about a year before the onset of this illness.

Examination.—On admission to the hospital the patient's temperature (by mouth) was 102 F.; the pulse rate was 80, and the respiratory rate, 20. The patient was tense and apprehensive and complained of severe frontal headache. Moderate rigidity of the neck and back was present, and Romberg's sign was positive. The achilles reflex was absent on both sides; the other tendon reflexes were diminished but equal on the two sides. Neurologic examination revealed otherwise nothing of consequence. Except for some dental defects and slight obstructive deafness bilaterally, general physical examination gave normal results. Cutaneous tests with old tuberculin, in a concentration of 1:100, gave negative results. A roentgenogram of the chest disclosed an area of calcification in the left lung, which was thought to represent a Ghon's tubercle, some fibroid, calcified areas in the left infraclavicular region and calcified glands in both hilar regions. Roentgenograms of the skull were normal except for calcifications in the choroid

Studies on the Cerebrospinal Fluid

	1937									1938			
Date	7/26	7/28	7/29	7/30	8/3	8/12	9/4	10/4	11/2	7/16	8/4	10/19	11/4
Turbidity	—	++	+	+	—	—	—	—	—	—	—	—	—
Pressure, mm. of mercury	12	6	8	4	6	18	10	16	15	12	14	10	10
Cells per cu. mm.	255	1,500	500	208	272	40	133	93	100	144	90	50	44
Neutrophils, %	52	88	30	30	18	27	7	9	20	19	24	2	45
Mononuclears, %	48	12	70	70	82	73	93	91	80	81	76	98	55
Protein, mg. per 100 cc.	95	127	..	..	151	..	180	217	179	174	246	200	..
Sugar, mg. per 100 cc.	38	..	..	..	42	45	32	24	23	Below 8	Below 8	Below 15	..
Bacteriologic findings (smear and culture)	Negative	Negative	Negative	Negative	Negative	..	Negative	..	Negative	..	..	Negative	..
Reactions for syphilis	Negative	Negative	..	..	..	..	Negative	..	..	Negative	Negative	Negative	..

plexus and pineal gland. Roentgenograms of the paranasal sinuses showed increased density in the lower portions of the antrums of Highmore, but otherwise nothing abnormal. No abnormalities were noted in gastrointestinal studies, the Graham-Cole test or intravenous pyelograms.

Cerebrospinal fluid obtained by lumbar puncture was examined on a number of occasions during the course of several periods of hospitalization. The results of some of these examinations are incorporated in the accompanying table; other examinations, the results of which are not included, gave essentially similar findings.

Bacteriologic studies of the spinal fluid were extensive and included, in addition to the usual smears and cultures, a search for higher fungi, as well as the inoculation of guinea pigs. None of the guinea pigs showed evidence of disease. Two laboratories reported negative reactions for syphilis, each making a complement fixation and a flocculation test.

Urinalysis gave persistently normal results. The highest leukocyte count on the blood was 9,100 per cubic millimeter, and this was obtained when the patient first came to the hospital; the lowest count was 6,000 per cubic millimeter. Smears of the blood showed from 65 to 78 per cent neutrophils and from 16 to 30 per cent lymphocytes. The hemoglobin concentration was normal. The sedimentation velocity of the red cells was normal. Blood cultures were repeatedly sterile.

Complement fixation and flocculation tests and estimations of the blood sugar and nonprotein nitrogen gave normal results. Agglutination reactions of the blood for typhoid, paratyphoid, melitensis, tularemia and dysentery were negative, as was the Weil-Felix reaction. Blood drawn approximately one month after the patient entered the hospital was sent to Dr. Charles Armstrong, of the National Institute of Health; he reported that the serum contained a strong concentration of antibodies against the virus of lymphocytic choriomeningitis.

Course.—The original impression was that the patient was suffering from meningitis or encephalitis of undetermined type. As a precautionary measure, sulfanilamide was given parenterally, daily, during one week of his stay in the hospital, and during this time the headache and cervical rigidity became less pronounced. The patient's temperature during the first few days in the hospital was "spiked," once reaching 104 F. and on several occasions 102 F. During the second week his temperature fluctuated for the most part in the vicinity of 100 to 101 F. (rectal), showing the greatest tendency toward elevation late in the day. He continued to complain of a constant frontal headache. The ordinary anodynes gave little relief, and codeine was necessary to control his discomfort. Stiffness of the neck disappeared shortly after the patient's admission. There were no other changes in the neurologic status. Although weak, he was up and about part of the time. Cells persisted in the cerebrospinal fluid; at no time were there less than 25 cells per cubic millimeter. Differential counts revealed chiefly lymphocytes, except in the first few examinations, when the polymorphonculears predominated. The protein remained high and the sugar content low. The patient was dismissed from the hospital as improved after three and one-half months, with a diagnosis of lymphocytic choriomeningitis. Samples of blood from six members of his family who were his immediate contacts were sent to Dr. Jerald G. Wooley, of the National Institute of Health, for examination for antibodies capable of neutralizing the virus of lymphocytic choriomeningitis. These studies gave negative results in each instance.

The patient was seen again, eight months later, at which time he reported that he had continued to have cephalalgia localized to the frontal and occipital regions, generalized weakness and nervousness. In addition he complained of mild equilibratory disturbance, tinnitus on the left, occasional epigastric distress and constipation. He had been incapacitated by the symptoms and could not work, although he was able to be up and about. He had been taking his own temperature and had noted an elevation of from 1 to 2 degrees F. late in the day. He appeared ill disposed, and was particularly distressed by his headache. General physical examination revealed no change, except that he was somewhat more gaunt than before. The neurologic abnormalities at this time were a positive Romberg sign, slight horizontal nystagmus on lateral deviation of the eyes, some stiffness of the back, absence of abdominal reflexes, a diminished patellar reflex on the left, absence of the achilles reflexes and slight impairment of superficial sensibility over the entire left lower extremity. He was hospitalized for almost two weeks. His temperature was normal in the morning, but was slightly elevated late in the day. Routine studies of urine and blood again gave normal results. Blood cultures were sterile. As indicated in the table, examination of the cerebrospinal fluid at this time showed persistence of meningeal irritation, as represented by pleocytosis, with a count of 144 cells per cubic millimeter, 81 per cent of which were mononuclears. In addition, the protein was still increased, and the sugar was extremely low. Blood was again sent to the National Institute of Health; Dr. Jerald G. Wooley reported that it contained a strong concentration of antibodies against the virus of lymphocytic choriomeningitis.

Two and one-half months later the patient was admitted to the hospital for the third time and remained for one month. His complaints were similar to those on the previous admissions. Physical examination revealed no additional changes except that superficial sensibility was now normal in both lower extremities. The usual studies of urine and blood gave essentially the same results as before, and the cerebrospinal fluid findings were of the same type. Except for occasional mild elevation, the temperature was normal during the course of this hospitalization. He continued to complain of frontal headache and generalized weakness. Phenobarbital was effective in reducing his distress, but the symptoms, nevertheless, interfered considerably with his activities. Neoprontosil (the disodium salt of 4-sulfamidophenyl-2-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid) was administered orally in doses of 5 Gm. daily, partitioned at equal intervals throughout the twenty-four hours, for two weeks, with no clinical improvement, although cerebrospinal fluid obtained on completion of this therapy showed a relative decrease in lymphocytes and a corresponding increase in the percentage of polymorphonuclears.

COMMENT

It becomes apparent from a review of the literature and the presentation of this case that the syndrome ordinarily described as benign lymphocytic meningitis may not always be mild and without disastrous eventualities. It is conceivable that in some cases in which complications or sequelae have been reported the authors may have been dealing with some other disease, perhaps either an abortive type of poliomyelitis or a meningeal type of epidemic encephalitis. Such possibilities have, of course, been suggested previously. It is to be noted, however, that in the cases reported by Findlay, Alcock and Stern and by Barker and Ford the virus of lymphocytic meningitis was shown to be present. It is hard to escape the conclusion, therefore, that the atypical features reported by these two groups of authors were associated with the specific type of lymphocytic meningitis and were not residuals of some other malady which had provoked a meningeal reaction. Evidence is slowly accumulating indicating that sometimes this variety of meningitis is not benign and that it occasionally results in chronic arachnoiditis or meningoencephalitis of severe nature. It is our impression that in the case we have reported the patient is now suffering from chronic meningoencephalitis which is a direct consequence of lymphocytic choriomeningitis.

CONCLUSIONS

1. A case of lymphocytic choriomeningitis is reported. Neutralizing antibodies protective against the virus of lymphocytic choriomeningitis (Armstrong) were found in the blood of the patient. One and one-half years after the onset of the illness, he still has definite signs and symptoms of chronic meningoencephalitis.

2. The literature dealing with the complications and sequelae of lymphocytic meningitis is reviewed, and a brief discussion is presented relating to the unusual forms of this malady.

CONVULSIVE AND OTHER NEUROLOGIC PHENOMENA APPEARING IN SENILE AND ARTERIOSCLEROTIC PSYCHOSES

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In a recent discussion of convulsive manifestations, the question was raised whether such phenomena occur in patients with the cerebral changes due to old age and its common companion arteriosclerosis. Since there was considerable disagreement of opinion and since little factual data could be found concerning this problem, it was thought to be one worthy of investigation.

The records of the McLean Hospital were used. The reports of 100 cases of cerebral arteriosclerosis and senile psychosis—representing two groups of consecutive admissions—were reviewed, with special attention to the nurses' notes.

Fifty-two of the patients were men and 48 women. Seven patients had generalized convulsions, most of which were repeated once or twice during the stay in the hospital. Four of these patients gave a history of cerebral accident at some time before or after the convulsive episode.

Two patients had what were described as "fainting spells," which involved loss of consciousness. Four patients had what were described as "dizzy" or "weak" spells, which did not involve loss of consciousness.

Three patients had prolonged coma, which in 2 patients lasted until death. One of the two patients lived one week; the other lived a year. The third patient has lived for four years and is still alive and comatose. In these patients gagging and gross defense movements were at times elicited. In the third patient it was possible during the early years of the coma to elicit an occasional answer of "yes" or "no."

SUMMARY

Of the group of 100 cases of senile and arteriosclerotic psychosis investigated, convulsions were shown in 7 per cent; episodic attacks which might be epileptoid, in 6 per cent, and profound and lasting changes of consciousness, in 3 per cent.

SPECIAL ARTICLES

OBJECTIVE TECHNICS IN PERSONALITY TESTING

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Ancient medical science based its diagnosis mostly on the observation of the patient under the conditions of life to which he happened to be subjected. During the last half century an enormous advance in the precision of medical diagnosis has been achieved by subjecting the various functions of the body to relatively invariable standard tests. For example, the condition of the pyramidal tracts is determined no longer entirely by the character of the patient's conscious muscular efforts but, in addition, by the nature of the plantar response to stimulus applied to the sole and by the tendon reflex as elicited by the percussion hammer.

THE NEED FOR OBJECTIVE PERSONALITY DIAGNOSIS

While the field of organic functions of the body has been increasingly well covered, medicine has been forced to recognize that the physical facts do not tell the whole story about the condition of the patient. It was by following a large group of arthritic patients for twenty years by means of all available physical diagnostic methods that Nissen,[1] in Boston, came to the conclusion that a psychologic factor is an important determinant in this organic disease. Dunbar[2] arrayed an enormous clinical material which demonstrates how all organic diseases are influenced, often in a decisive way, by the psychologic condition of the patient.

This new development in medicine puts before the psychiatrist the task of bringing medical psychology up to the level of objective diagnosis which has been recognized and partly achieved in organic medicine. At present one finds medical psychology in a situation similar to that existing in organic medicine up to the middle of the last century. The analytic work of Freud and of those influenced by him has furnished many shrewd and subtle observations on the working of the conscious and the unconscious mind. Ancient physicians were in many respects superior observers of the symptoms and clinical course of organic disease. When it comes, however, to the point where these stimulating discoveries

1. Nissen, A.: Chronic Arthritis and Its Treatment, New England J. Med. **210**:1109, 1934.

2. Dunbar, H. F.: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1933, New York, Columbia University Press, 1935.

should be applied by the physician in his practical dealing with the individual patient, those not trained in modern psychopathology find themselves in an unsatisfactory position. There are many conflicting theories in the field. Emotional difficulties are successfully cured by the use of suggestion, by orthodox freudian procedures and by the methods of Stekel, Rank, Adler and Jung. Every psychologic system appears consistent in itself, but in order to appraise the individual patient on the basis of any of them a highly specialized training is entailed. The modern-minded practitioner feels the want of psychologic standards by which he may compare the psychologic makeup of the patient with that of others he knows and, furthermore, with the findings of other observers.

One might think that some day the different psychologic schools of thought might reach an understanding and all speak the same language. But patients cannot wait until this agreement is reached, and it is probable that one is still far from such achievement. The reason for this is that all the different theories operate on the basis of certain social, national, religious and ethical values which contributed to the personality of the founder and which are consistent with the personalities of his followers. Until humanity has reached the status of standardization which Aldous Huxley described in "Brave New World" there will always be individual differences between men rooted deepy in their inherited organic structures. It has been one of the most meritorious contributions of Jung [3] to medical psychology that he demonstrated the futility of all the fights between the various religious, philosophic and psychologic thinkers. Whenever fundamental spiritual values are involved, objective truth or falsehood cannot justly be made an issue, because the same objective situation appears different to observers with a different personality makeup. Every human being, healthy and normal as he may be, has his strong and his weak points and cannot help appraising everything according to the construction of his individual power of perception. The predominant extravert cannot make use of the principles which may guide an introvert through life in a perfectly satisfactory way, and vice versa. A typical Englishman cannot direct his life successfully by following the behavior pattern which works for a German.

If one delves thus into the individual side of psychology, the case looks rather desperate for an objective approach to medical psychologic problems. But one must remember that the different theoretic approaches to human psychology have developed out of therapeutic efforts in behalf of psychoneurotic persons. There the problem centers around an individual scale of values. It is because the highest level of the psychologic attainments of man is involved and because psychoneurotic disturbances proceed from this level that medical psychology seems to lack objectivity.

3. Jung, C. G.: Psychological Types; or, the Psychology of Individuation, New York, Harcourt, Brace and Company, 1923.

There are, however, vast realms within the structure of human personality and behavior which can be studied objectively without implicating the conflicts between superego, ego and id. The more one studies the psychologic disturbances of persons suffering from organic ailments the more one becomes aware of the fact that the exaggerated individual differences in personality found in neurotic and psychotic patients obscure insight into other fundamental elements of personality. I refer to the fact that important psychologic similarities are found in groups of patients in which a specific organic system, such as the extrapyramidal, vasomotor, respiratory or gastrointestinal, exerts an outstanding physiologic or pathologic influence on the life of the person. In other words, there is a rich field to be exploited between the individualistic psychoanalytic approach and that expressed in Kipling's lines:

> "The colonel's lady and Judy O'Grady
> Are sisters under the skin."

At least, persons suffering from arthritis, hypertension, peptic ulcer, migraine and tuberculosis are much alike under the skin. The personality types found in such groups represent the most important field of objective testing in modern medical psychology.

What is meant by "objective testing" of personality? The same as in organic medicine, namely, that the patient's reactions to a standard situation are observed and that the individual differences of reaction can be measured. It is important that the patient be as unaware as possible of the significance of his reaction and that the examiner be enabled to submit his results to others for control both of the facts and of the conclusions he has drawn from them. More one cannot do even in organic medicine, in which occasionally one must cope with expert malingering and not infrequently encounter difficulties in drawing definite conclusions from objective data. It is obvious that the questionnaire method does not fulfil the exigencies of the problem, because with it the patient knows at once what his responses indicate to the examiner. Few people are honest enough, even toward themselves, to face their shortcomings, much less to state them to the physician without trying to make things look nicer than they are.[4]

Recently, two methods have been developed and put into practice which fulfil in a satisfactory way the requirements of objective recording of personality traits: the analysis of handwriting and the Rorschach test. I wish to stress the point that in both methods one deals at present

4. Syz gave a questionnaire to 64 medical students regarding their emotional reactions to certain words. They reported that they were affected emotionally by the words "father" and "mother" but not by "intercourse" and "lazy." During this test the psychogalvanic reaction of the subject was recorded and showed the opposite of what the subjects said (Syz, H. C.: Psychogalvanic on Sixty Four Medical Students, Brit. J. Psychol. **17**:54, 1926).

primarily with the quantitative recording of individual differences in basic personality traits. In this respect both methods are technically objective. The interpretation of the graphologic and Rorschach scores still offers many unsolved problems and stands in need of greater clinical experience. It is in order to stimulate interest in this direction that I have undertaken this survey of the situation as it exists at present. May I add that the difficulties of an objective interpretation of handwriting and of the Rorschach test are due not wholly to shortcomings of these methods but to a great extent to the fact that there is still so little known about the structure of personality and its objective evaluation?

THE ANALYSIS OF HANDWRITING

Of the two methods the analysis of handwriting is the older. It is based on the simple observation that every member of a national group learns to write after the example of the identical school copy, but that immediately each person departs from this standard pattern. That these departures from the common school copy are definitely characteristic of the individual person has been recognized by courts of law. The objectivity of personality characterization by handwriting is based on three facts: (1) Every person of the same national group is presented with the identical task: to write according to the common school copy of the country; (2) every person deals with this task in his own, characteristic way; (3) the difference between the school copy and the individual handwriting can be measured and described objectively.

The most fundamental characteristics of handwriting will be mentioned in the following outline:

1. Elements capable of precise measurements.
   - (*a*) The height of letters of middle length, which serves as the indicator of the size of the writing; letters, such as m, above ⅛ inch (0.32 cm.) are considered large writing, those below small writing.
   - (*b*) The upper lengths and under lengths and their relative proportions.
   - (*c*) The proportionate size of letters beginning and ending words, sentences and whole documents as compared with the rest of the writing.
   - (*d*) The width of the letters, which is measured by the width of the upper loops in such letters as *l*, *b* and *t*.
   - (*e*) The width of the writing, that is, the distance between single letters. "Narrow writing" means that the distance between the letters is less than the height of the short letters; "wide writing" means that this distance is greater.
   - (*f*) The degree of the slant, by which is meant the angle formed by the downstroke with the horizontal line.
   - (*g*) The straightness or curvature of the lines.
   - (*h*) The degree of the angle formed by the writing line with the horizontal line.

2. Elements capable of statistical evaluation.
   (*a*) The amount of regularity with which the measurable factors appear—in particular, the regularity of height, width and slant of the letters and the use of specific connecting forms.
   (*b*) The prevalence of a tendency toward the right or the left in writing. By this is meant whether, in comparison with the school copy, strokes in the one or the other direction are added or omitted.
   (*c*) The degree of connection between the letters: If more than four letters in a word are written without interruption of the stroke the handwriting is considered to be "connected"; if less it is considered to be "unconnected."
3. Formal relation to the school copy.
   (*a*) The letters are either formed carefully according to the school copy or are simplified or amplified, or the forms of single letters may be exchanged for one another. For a person who exchanges forms of letters there is a German colloquialism: "He makes an 'x' for a 'u.'"
   (*b*) The downstrokes in letters like *m, n,* and *u* are connected either according to the school copy or, independently of the school copy, in the form of garlands, arcades, double curves, threads, double angles or supported angles.
   (*c*) The pressure of the stroke may be either strong or weak; it may be placed in downstrokes, according to the school copy, or it may be misplaced in side strokes.
   (*d*) The quality of the stroke may be either sharp or "pasty," according to the angle between the pen and the paper.
4. Speed of writing.

An important factor in handwriting can be judged only indirectly, namely, the speed of the handwriting. There are twenty-six criteria for the rate at which the specimen has been written. These are:

Indications of Speed	Indications of Slowness
1. Uniformity of slant	Change of slant
2. Increase of slope	No change in slope
3. Widening of the left margin	Left margin vertical
4. Wide writing	Narrow writing
5. Wide letters	Narrow letters
6. Simplified letters	Carefully drawn letters
7. Sharp strokes	"Pasty" strokes
8. Garland and thread connections	Double angles and double curves
9. Increased tendency toward the right side	Increased tendency toward the left
10. Sharp, outgliding end strokes	Lack of end strokes, or end strokes turned toward the left side
11. Dots for *i*'s shaped like commas	Round dots for *i*'s
12. Dots for *i*'s set ahead of writing	Dots for *i*'s set exactly above the downstroke of the *i*
13. Clear, smooth strokes	Uncertain strokes

These are empiric rules for the evaluation of speed, and to a certain extent, too, the evaluation of pressure is made indirectly. It is therefore necessary to emphasize that the validity of these rules has been corroborated by experimental methods, notably, the "scales of writing" (*Schriftwage*), which were introduced by Kraepelin, and, more recently, the "graphodyne" of Roman-Goldzieher. There are additional characteristics of handwriting which I have not enumerated, since they are more complex and therefore not so susceptible to generalized expression.

The psychologic significance of the various component factors in handwriting is based partly on empiric observation, partly on the fact that all motor activities not only are purposive but express instincts and emotions. The development of scientific graphology corresponds roughly to the development of modern neuropsychiatry. First, the French in their classic manner began to observe and describe neatly the characteristic traits of handwriting which belonged to persons showing certain outstanding psychologic traits, such as elation or depression, honesty or dishonesty, self control or impulsiveness and modesty or pride. The reasons for these empiric interrelations between handwriting and character could not be clarified by this approach, just as Janet did not go deeply into the causation of the psychoneurotic symptoms which he described so competently. But as Janet's approach was followed by Freud's psychobiologic interpretations, so the dynamic basis of graphology was clarified by Klages [5] (Stein-Lewinson).[6] Klages recognized clearly that the human mind is not expressed in speech and purposeful action alone. The rationalistic modern person is inclined to think so, but in reality human beings express themselves and understand each other to a large extent by means of somatic manifestations, such as gestures, postures and facial expression. Not only does every one do these things instinctively, without any practical purpose, but even purposeful actions are modified in characteristic ways by the personality. Kretschmer [7] and his school have investigated this problem exactly by means of experimental psychologic methods. When schizothymic and cyclothymic groups were compared with respect to finer differences in execution of identical physical tasks typical characteristic differences between the two groups were found. This expressive component participating in one's every action accounts for the fact that every person's handwriting deviates from the school copy in a way characteristic of the person himself. Klages [5] demonstrated the similarity between the expressive movements of daily life, which everybody understands, and the corresponding modifications of the standard school copy. Persons who add unnecessary loops and

5. Klages, L.: Handschrift und Character, Leipzig, Johann Ambrosius Barth, 1919.

6. Stein-Lewinson, T.: An Introduction to the Graphology of Ludwig Klages, Character & Personality **6**:163, 1938.

7. Kretschmer, E.: Körperbau und Character, ed. 12, Berlin, Julius Springer, 1936.

flourishes to their writing will be found inclined toward exaggeration and affectation; persons whose downstrokes slant to the left are inhibited in following their impulses; asthenic persons display little pressure, and forceful persons much; sensuous persons produce a "pasty," and frigid persons a sharp, stroke. I have given these few examples reluctantly, in order to illustrate the general principle of interpretation, because the value and importance of an isolated graphologic indication can be judged not by itself alone but only in association with all other characteristics of the same handwriting. An isolated symptom of secretiveness, for instance, does not indicate a thoroughy insincere person, but means only that this man, like most people, will not expose everything in his private life to the general public. It has been empirically established that only if there are more than four indications of secretiveness must one consider the person more insincere than the average. In order to find out whether the subject is a repressed neurotic person, a pathologic liar, a thief or an unscrupulous business man, all the other indications of the handwriting must be taken into consideration. The two to four hours which are required for a graphologic character analysis are spent chiefly on the task of grouping indications with correlated characterologic significance and of balancing them against other groups of indications with a corresponding meaning.

It may be objected that there is too much speculation in the interpretation of handwriting as an expressive phenomenon, that too much is taken for granted in assuming such a close correlation between expressive movements in daily life and individual modifications of the school copy. It is therefore important to point out that these seemingly speculative conclusions have been validated empirically to such an extent that they can be accepted as facts. It is unfortunate that, so far, nearly all serious graphologic work has been done in Europe, especially in the countries in which the French and German language is spoken where graphologic analysis has been used so extensively in business life, in medical and legal practice and in research work that it is taken seriously by critical and responsible people. The third International Congress of Graphology, which took place in Paris in 1937, was attended by many outstanding men of the medical profession and was opened by Pierre Janet, who is honorary president of the French Graphological Society.

Recent developments in graphology have served to strengthen confidence and to deepen understanding of the method. I refer to the work of Schönfeld and Menzel [8] in Czechoslovakia, and of Stein-Lewinson,[9] in the United States. Their research work on such organic diseases as

8. Schönfeld, W., and Menzel, K.: Tuberkulose, Charakter und Handschrift, Brünn, Rohrer, 1934.

9. Stein-Lewinson, T.: Die Handschrift des chronischen Arthritikers, Schrift **3**:114, 1937.

pulmonary tuberculosis and chronic arthritis revealed that these diseases, which do not necessarily affect the act of writing mechanically, are still expressed specifically in the handwriting. In pulmonary tuberculosis a certain change in the breathing function occurs. There is a diminution of the "reserve capacity" of the lungs. Parallel to this change in reserve capacity the following symptoms appear in the handwriting: (1) wavering and disconnected upstrokes; (2) broken downstrokes; (3) breaking and flattening of normally oval forms; (4) breaking of the loops in the upper and under lengths, and (5) rest stops.

In the handwriting of arthritic persons seventeen specific symptoms were found which correspond to the constitutional makeup of the potential arthritic subject. Of these, six traits undergo typical changes after the onset of the disease process, and these changes are consistent with psychologic changes as observed by other methods. This suggests that the determinant factors of handwriting proceed from the organic biologic level. One is safe, therefore, in assuming that handwriting not only reveals superficial character traits but reflects dynamic changes in the biologic structure of the organism. In other words, the characteristics of handwriting are based not on the conscious thinking of the writer and the condition of his motor apparatus but on his integrated psychosomatic structure. This illustrates and supports the work of Lewis,[10] who has insisted for many years on the shortcomings of medical psychology, which emphasizes only the brain and the endocrinal system as important factors in human psychologic reactions. The results of the studies on patients suffering from pulmonary tuberculosis suggests that graphologic analysis is a valuable method for the investigation of the psychologic aspect of all organic disease.

THE RORSCHACH METHOD

The Rorschach method is much younger than graphology. Rorschach's book entitled "Psychodiagnostik," [11] was published in 1921. This means that considerably less practical experience has been had with this method than with graphologic analysis. Unlike it, however, the Rorschach method has been developed with psychiatric problems in view and has been tested from its beginning on patients in psychiatric institutions in Switzerland. The work was begun at the famous "Burghölzli" clinic of Bleuler, in Zurich, Switzerland. Graphology, on the other hand, has been built up with problems of normal psychology and behavior in view and encounters more difficulties in meeting the demands of medical psychology. It is unfortunate, therefore, that since the untimely death

10. Lewis, N. D. C.: A Discussion of the Relationship of the Chemical, Physical and Psychological Aspects of Personality, Psychoanalyt. Rev. **11**:403, 1924.

11. Rorschach, H.: Psychodiagnostik, Bern, E. Bircher, 1921.

of Rorschach, in 1922, the profession at large has not paid the attention to his labors that they merit. The work which psychologists, teachers and pedagogues have done with the Rorschach method has not led to entirely satisfactory results. Beck,[12] for instance, recently approached the personality problem from the point of view of so-called normal behavior and intelligence, making the Rorschach method in fact a complicated intelligence test. This it is definitely not meant to be. In reality the method is concerned with the instinctual and emotional factors on which normal social and intellectual behavior is based.

The testing material consists of a set of ten white cards on which five black and five multicolored ink blots are reproduced from the originals with which Rorschach did his experimental work. These cards are exhibited to the patient one after the other, and he is requested to tell what they look like to him. The cards are actually placed in the patient's hands, so that he may look at them from any aspect that he chooses. His responses are put down in writing, and only after the patient has completed the whole set is he asked questions regarding such responses as need clarification. Experience has shown that no two persons see all the ten ink blots in an identical way, although some responses enjoy a great popularity. The shape and outlines are all indefinite enough that they do not force a fixed interpretation on the subject but allow him a wide margin for individual reactions. His responses are accepted as given and are not in any sense judged as correct or incorrect. The objectivity of the results is guaranteed in a manner somewhat similar to that in the graphologic method, since the conscious attention of the subject is preoccupied with the contents of what he is writing or seeing and he is not aware of the formal principles involved. As a matter of fact, the preoccupation with the contents makes it nearly impossible even for the graphologist or the Rorschach expert to mask his true personality when he himself is the subject. As a rule, the patient who takes the Rorschach test is under the impression that either his fantasy or his intelligence is being put to the task of discovering similarities between the ink blots and real objects. Contrary to this conception, however, the contents play only a secondary role in the interpretation.

The scoring of Rorschach records, like the analysis of handwriting, is concerned primarily with formal characteristics of the responses. The chief categories of the Rorschach score are as follows: 1. Responses are classified with reference to the part of the card to which they refer, viz., whether the individual response relates to the whole blot or to details of it. Responses to details can be classified according to whether they refer to larger or smaller parts of the blot. Another classification is based on whether the outline of the blot or the lines in its inner shading are emphasized. Some patients display a tendency to interpret the white spaces between parts of the ink blot instead of the ink blots proper. Finally, the respective sums of all these categories are computed.

2. Responses are classified according to their emphasis on outline or surface of the ink blot. When outline determines the response, it is again differentiated on

12. Beck, S. J.: Introduction to the Rorschach Method: A Manual of Personality Study, with Preface by F. L. Wells, Monograph 1 of the American Orthopsychiatric Association, Menasha, Wis., George Banta Publishing Company, 1937.

the basis of its static or dynamic quality. A static, pure form response for card I is "crown"; a typical movement or dynamic response for card VII is "two scolding women." Between these two extremes, it is useful to differentiate responses concerned with a scale of movements ranging from passive to active—e. g., "stones thrown out by a volcano," "a pointing hand," "an animal climbing," "clowns performing a dance."

When the surface of the blot influences the response, one must distinguish responses determined by the shading from those determined by the colors. The latter may be pure or they may be more or less influenced by outline. For example, a typical shading response for card VI is "fur rug"; responses for the same red detail in card III in which the color element plays a role to different extents are: "blood," "flames in a fireplace" and "a red bow tie."

An important type of response is the so-called chiaroscuro response. By this is meant a response in which the shaded surface of the blot acts as a determining stimulus but in which the subject experiences an additional element of depth, of tridimensional space. For example, clouds, smoke, scenery, roentgen pictures or a relief map may be mentioned. Such interpretations must be considered a synthesis of a response to a surface stimulus and a kinesthetic reaction of a rudimentary type. That there is a functional relation between tridimensional perception and kinesthetic function is perhaps not self evident, but has been proved by psychologic experimentation and observation in cases of tactile gnostic disturbances (Cohen [13]).

Finally, the respective sums of all the different types of responses concerned with outlines and surface are computed.

3. The responses are classified according to their reference to the following categories: human beings and animals; the whole or parts; anatomic structures, plants, scenery, architecture, objects and abstractions. Again, the sum for each class of responses is computed.

4. The percentage of responses of a popular type and that of responses of an unusual character, so-called originals, are estimated. The former category occurs in about one third, the latter in 2 per cent or less, of all records. In addition to these, the percentage of animal responses is computed. These are as a rule the most frequent interpretations.

With the figures for all these variables in hand, the formal description of the personality is possible. It is based on both the absolute figures for the several scoring points and the quantitative correlations between them.

The psychologic interpretation of the Rorschach score makes use chiefly of two principles. One is based on the correlation between well defined psychologic traits and elements in the Rorschach score. The other principle makes use of the fact that the significance of every type of reaction changes with the specific card for which it occurs.

The following outstanding psychologic correlations have been discovered in the Rorschach score.

1. The broad distinction between responses prompted by outlines and those prompted by surfaces of the blots corresponds to the distinction between intro-

13. Cohen, G.: Sterognostische Störungen, Deutsche Ztschr. f. Nervenh. **93:** 228, 1926.

versive and extraversive tendencies in the personality makeup. By introversive tendencies are meant the tendencies in the personality which aim at an independent, individualistic way of living. The more emphatically the introversive factors appear in the score the stronger the urge of the subject to create and do things according to his own inner conceptions and aims. By extraversive tendencies are meant the affectibility of the subject by his environment. Chiaroscuro responses, which represent a primitive mixture of surface and movement factors, are indicative of a chaotic condition of the mind in which neither the subject nor the environment is capable of assertion in a differentiated way.

Differentiated introversive responses range from pure form responses, which are indicative of conscious, intellectual control, to those concerned with human movement, which reveal independent and creative capacities. Form responses, with a more primitive element of movement in addition, signify undeveloped introversive capacities.

Extraversive responses range from texture responses, corresponding to the level of physical, sensuous excitability, and color responses, indicating emotional affectibility. If the response shows a balance between form and color emotional adjustment is indicated. With the weakening of the influence of form the rational control of emotions weakens correspondingly. In psychotic and epileptic persons one finds pure color responses, e. g., "sea water" for the green part of card IX.

In normal persons one finds a certain number of both movement and color responses. If both are lacking one speaks of a coarctation of the experience balance. This is evidence of a loss of both initiative and emotional responsiveness and is found in persons with compulsion neuroses and endogenous depressions.

The type of intellectual approach to life is evaluated by the degree to which the responses are concerned with the whole ink blot, with large or small details or with the white spaces. Responses concerned with the whole blot indicate a tendency to grasp and take into account the total situation, a propensity which is found in domineering and ambitious persons, in creative artists and in theoretic thinkers. Responses concerned with larger details, which are much easier to give, indicate a capacity to deal with the practical side of life, regardless of large issues. The smaller the details in the response the stronger the tendency of the subject to lose himself, without an integrated attitude toward life. They are found in the scores of schizophrenic persons and pedants with compulsion neuroses.

A peculiar attitude toward life manifests itself in responses referring to white spaces. Evidently, people responding in this way display their intellectual capacities without reference to the actual task symbolized by the ink blot. Such responses, especially if more than one occurs in a record, betray a tendency to escape from a task with which the person tested feels incapable of coping. At the same time the subject avoids admitting his weakness and covers it up by rationalizations and wishful thinking.

The distribution of responses among the various contents indicates mainly the trend of interests of the person, either directly or symbolically. One may expect that a person who finds no human figures in the ten cards has probably failed to form proper human relations; plants are seen frequently by children and adults with infantile personality traits; scenery and objects are often evidence of the preoccupation of the patient, especially if they take the place of human responses. The same holds true for responses dealing with sexual organs, which are found in sexually maladjusted persons.

With regard to the significance of the percentages of popular and of original responses: It is obvious that the percentage of popular responses is proportionate

to the degree to which the subject is capable of seeing things in a conventional way, while original responses correspond to the presence of an individualistic attitude. Odd characters are most likely to have many original and no popular responses.

The meaning of the percentage of animal responses is related to the fact that for a normal person it is easiest to see animals in these cards. Only persons with either a very volatile or a rich mind see animals in less than 35 per cent of the blots. The higher the percentage of animal responses the greater the inertia of the mind. An average percentage of animal responses is an indication for a normally stable way of thinking.

An important correlation exists between the number of responses concerned with the whole blot and the number concerned with human movement. Normally one finds a proportion of 2:1. An excessive number of the former responses betrays an ambition which overtaxes the psychologic capacities of the subject. An excess of the latter over the former type is found in egocentric persons who are more concerned with their own selves than with the world in which they live. There are many more correlations between the many variables of the Rorschach score, but it would lead too far to dwell on them.

The second principle of interpretation to which I have referred is based on the type of responses as they are given to each individual card. Each card is constructed with the idea that it should make a particular category of responses easy and others difficult. It is therefore important to note whether certain forms of responses are given to cards which make them difficult and other responses are missed although the particular card apparently should make them easy. With regard to this principle of interpretation the ten cards may be described as follows:

CARD I.—Whole and detail responses, form and movement responses and shading responses are all made easy.

CARD II.—Red is introduced. For persons with well integrated emotional responsiveness it is easy to combine the red and black parts into a whole and a movement response. Persons who are easily disturbed by emotions are able only to see details, or may even fail to respond at all. In this case one describes the reaction as "color shock." Furthermore, the definite white space in the middle gives an opportunity for a white space response.

CARD III.—In this card it is made particularly easy to see human beings in action, while the red color is distributed in such a way that it might easily be disregarded.

CARD IV.—Here the black shading provides the most outspoken stimulus and readily disturbs persons who are inclined to react with depressive swings in mood.

CARD V.—Detail and movement responses are made particularly difficult.

CARD VI.—The outstanding stimulus in this card is the shaded surface, which suggests a furry texture to most people. Furthermore, the upper part easily suggests a phallic symbol.

CARD VII.—This card is apt to stimulate pure chiaroscuro responses, such as "smoke" or "clouds." For those not inclined to react in this way responses concerned with human movement and with details of form are readily suggested. Furthermore, opportunity for a large white space response is provided.

CARD VIII.—Here, for the first time, all the ink blots are in colors. At the same time, it is made easy to distinguish the figure of a climbing animal, except in cases in which the patient is disturbed by a color shock.

CARD IX.—While the preceding card is made up in harmonious and bland colors, the colors in this card are disagreeable and disharmonious. They provide a special opportunity for persons disposed to react with excessive emotional outbursts. Here, again, a white space reaction is made easy.

CARD X.—This card is made up in a great many gay colors and gives many opportunities for detail responses, but makes whole responses and human movement responses rather difficult.

These indications are sufficient to point out how extremely rich are the opportunities for a highly differentiated expression of personality in the Rorschach test. In order to illustrate the fact that the Rorschach score actually brings basic trends of the personality into evidence, I wish to characterize a few typical Rorschach findings in groups of patients with well defined organic disease. I choose organic diseases because there appears to be a similarity in the psychobiologic constitution of patients affected by the same organic disease. Studies of the personality background of persons with organic disease suggest that the latter represents a regressive expression of dominant premorbid personality traits (Booth).[14]

A striking example can be found in the results of the Rorschach test with patients affected by the two stiffening diseases: paralysis agitans and chronic arthritis. In both groups one finds the tendency toward whole responses far in excess of human movement responses. This indication of a strained attitude toward the environment corresponds to the rigid personality of the premorbid period, later expressed in physical rigidity and/or stiffness. The difference between the Rorschach records of the two groups is expressed in the different quantitative relation between responses concerned with human movements and those with color. In cases of paralysis agitans the values for color and movement responses are about equal, and the patient appears to be stimulated by the color influence. This indicates the tendency to be activated by emotional influences coming from the environment and corresponds to the clinical observation that patients with this disease are likely to lose their rigid immobility under the influence of emotions. In cases of chronic arthritis the color responses are either lacking or inferior in number to the movement responses. Often the colors prove a definitely disturbing factor, and a typical color shock is displayed. This means a defensive attitude against emotional involvement and outside influences, a peculiarity of the arthritic personality which is responsible for the passive resistance of this group of patients to all sorts of therapy (Booth [14]).

14. Booth, G. C.: Personality and Chronic Arthritis, J. Nerv. & Ment. Dis. **85**:637, 1937.

In the cases of the two diseases just mentioned color responses never exceed whole responses in number, and in cases of paralysis agitans only rarely and to an inconsiderable degree do they exceed movement responses. This means that outside stimulation is not able to disintegrate the total personality attitude and that action, if any, fits the personality pattern. In contrast to this, one finds in the group of patients with chorea minor (Krauss,[15] Bruch [16]) that color responses definitely exceed movement responses and often approximate, or even exceed, whole responses. These facts suggest that outside stimulation easily overrules the intentional action pattern of the subject and eventually disintegrates the personality structure. This corresponds to the type of aimless hypermotility which characterizes the acute stage of the disease and to the psychologic hyperexcitability and psychasthenia which are found in these patients many years after the acute, somatic symptoms of the disease have disappeared. An additional indication for the lack of purposive control, which is characteristic of this group of patients, appears in their Rorschach records, namely, a definite tendency to react to shadings and white spaces instead of to the outlines of the ink blots. Not only in their motor responses but also psychologically patients with chorea minor are inclined to miss their normal objectives.

In patients with cardiovascular disease a preference is found for responses prompted by detail, and relatively little attention is given to the whole ink blots. This indicates the failure of these patients to develop an integrated attitude toward their environment and their preoccupation with isolated, momentary issues. A similar condition is found in the Rorschach records of persons affected by states of fear and anxiety. Again, this result of the Rorschach test is in harmony with the psychologic studies of Wolfe [17] and Menninger.[18] These authors found that cardiovascular patients are characterized by lack of a conscious emotional attitude toward their situation in life at large. Although they describe situations which naturally would provoke resentment, they deny the existence of such emotions in their consciousness. The authors explain these findings by the existence of a strong repression of aggressiveness. Actually these patients rely on support by traditions, institutions and persons rather than on their own strength, as patients in the arthritic and parkinsonism groups do (Booth [14]). There is ample evidence that peoples bound by custom and tradition, such as Negroes, Chinese and Egyptians

15. Krauss, S.: Persönlichkeitsveränderungen nach Chorea minor, Schweiz. Arch. f. Psychiat. u. Neurol. **34**:94, 1934.

16. Bruch, H.: Personal communication to the author.

17. Wolfe, T. P.: Dynamic Aspects of Cardiovascular Disease, Am. J. Psychiat. **91**:563, 1936.

18. Menninger, K. A.: Emotional Factors in Hypertension, Bull. New York Acad. Med. **14**:198 (April) 1938.

(Ismail [19]), do not acquire hypertension in their native environments, but do so readily under the impact of the overpowering, aggressive civilization of modern white man. It seems as if the relation between an unacceptable environment and cardiovascular disease did not escape the observation of the old Hebrews. At least, one finds in the Fifth Book of Moses (chapter 23, verses 64 to 67):

> And the Lord shall scatter thee among all people . . . and there thou shalt serve other gods, which neither thou nor thy fathers have known . . . And among these nations . . . the Lord shall give thee there a trembling heart and failing of eyes . . .: And thy life shall hang in doubt before thee; and thou shalt have fear day and night, and shalt have no assurance of thy life.

DIFFERENCE IN SCOPE BETWEEN ANALYSIS OF HANDWRITING AND THE RORSCHACH METHOD

Although both methods, the graphologic and the Rorschach, are competent instruments of objective personality study, there exist theoretic and practical differences in the use of them. One difference is based on the fact that a separate aspect of personality underlies each method. Both methods may be described as a projection of the personality into a simplified and standardized environmental situation (Piotrowski [20]). One might compare the essence of the procedure to the projection of a tridimensional object on a plane surface, which gives, of course, somewhat different pictures according to the angle and side of the object projected. Two different projections may picture an identical object, but for practical reasons sometimes one, sometimes the other, projection may be more useful.

In the graphologic method, the school copy represents the average character of the collective social environment. It is hardly necessary to mention that the school copies of different countries have a distinct relation to the average national character. The individual person denotes his particular character by the distinctive way in which he modifies the standard school copy.

In the Rorschach procedure, the five black and the five variegated ink blots, with their vague and protean configurations and shadings, represent the objective environment in which all live. To the infinite possibilities which both real life and these ink blots offer for active, emotional and rational responses the individual subject reacts selectively, according to his particular dynamic makeup.

Because of these methodologic differences, handwriting is apt primarily to reflect the active side of the personality, while the Rorschach

19. Ismail, Abdel-Aziz: Aetiology of Hyperpiesis in Egyptians, Lancet **2**:275, 1928.

20. Piotrowski, Z.: Methodological Aspects of the Rorschach Personality Method, Quart. Psychol. **9**:29, 1937.

record expresses the manner in which the person experiences his environment. Each method, however, may express something of both. But one must distinguish that in each one deals with one side of the personality full face, so to speak, while the other side is seen only in profile. For example, the graphologic method will show clearly that a person lies, and in what way and in what respects, while the Rorschach record will indicate with equal clarity the mode of inner experience which forms the background of this behavior.

Other differences regarding the use of these methods are of a practical order.

The graphologist is largely independent of the subject's cooperation, since he can use material produced without knowledge of the fact that it will be used for an analysis of personality. Furthermore, he can follow up the life history of the patient and note the periods in which important changes have taken place.[21] Besides the analysis of the patient's personality, the graphologic method makes possible a study of the character of people who may have influenced his life.

The Rorschach method depends on the willingness of the patient to cooperate, but this is not so much of a shortcoming in practice because it is only rarely that any one balks at the procedure. That people occasionally leave out one or another embarrassing idea plays no important role because the general pattern of the record does not depend on single responses. Besides, an experienced and watchful observer easily notices indications of such holding back of material and can encourage the patient later to say it by asking him point blank if at this or that moment of the test he withheld any impression.

A particular usefulness of the Rorschach method can be found in its application to psychotherapy. Before one begins psychotherapy, one can determine fairly well whether the patient is open to psychologic treatment at all and whether the approach must be suggestive or psychoanalytic. In the course of psychoanalytic treatment it is often difficult to determine whether or not the patient responds in a positive way because the outward symptoms are liable to stay considerably longer than the inner attitude which brought them into existence. When the usefulness of continued analytic treatment is in doubt, repetition of the test may give valuable clues to the inner condition of the patient.

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21. For instance, I observed a patient who insisted that the severe arthritis of the hip joints from which she suffered began shortly after the birth of her first child. From examination of the handwriting of her diaries, however, I was able to point out that the arthritis must have begun ten years before the birth of the child. She then recalled that at that time she had been greatly troubled by pains in the hips, but that nobody had paid attention to her complaints because they were considered "growing pains."

It is hardly necessary to dwell on the importance of both methods for personality studies in all sorts of functional and organic disease, but I wish to point out their enormous value in the fields of mental hygiene and prophylaxis. That psychotherapy is usually such a highly individualized and costly procedure may be partly attributed to the fact that patients do not come for help until they are seriously disturbed. Behind a mask of apparent adjustment they may have worked themselves into complicated external situations, which are in many instances irretrievable. At an earlier stage it might have been easy to help such persons by psychologic counseling. Vocational guidance and premarital consultations could improve on their success considerably, if psychiatrists would make use of reliable methods of personality examination. I have no intention of depreciating the importance of physical examinations and of the usual psychologic tests, but they cannot prevent the misery which so often comes from neglected personality maladjustments. The experiences of Hackfield [22] and others have demonstrated that people may be benefited by courses in mental hygiene more economically and more efficiently than by individual therapy if they have not regressed too far.

SUMMARY

1. Growing insight into the personality factor in the causation of all sorts of organic and functional disease makes it of paramount importance for modern medicine to establish objective criteria in the examination and diagnosis of personality.

2. Two methods of objective personality examination are available and have proved reliable: (*a*) the analysis of handwriting, which approaches the person from the side of his action pattern and is apt to reveal the various organic factors which mold and influence his personality; (*b*) the Rorschach method, which records the inner attitude of the person toward life, his constructive and reactive tendencies and his intellectual control. The total constitutional makeup of the subject is reflected in the absolute figures and their correlations as they appear in the many variables of the Rorschach score.

3. Handwriting analysis and the Rorschach method are both valuable aids to the physician. They give the general practitioner insight into psychologic difficulties in the life of patients suffering from organic disease which otherwise could be discovered only by lengthy and expensive psychiatric explorations. For the neuropsychiatrist they are particularly useful in determining objectively the choice of psychotherapeutic approach and the probable response of the patient to the method chosen.

22. Hackfield, A. W.: Can a Reorientation Mass Therapy Correct the Fallacious Concept of the Incurability of Mental Disease? J. Nerv. & Ment. Dis. **86**:39, 1937.

Abstracts from Current Literature

Physiology and Biochemistry

THE RELATIVE SPEED OF FORMATION OF LECITHIN AND CEPHALIN IN THE BODY. ERWIN CHARGAFF, J. Biol. Chem. **128**:587, 1939.

Chargaff found that the intestinal tract synthesizes lecithin at almost twice the rate that it does cephalin. Brain, on the contrary, synthesizes these phosphatides at almost equal rates. To demonstrate this, he employed the Hevesy radioactive phosphorus method, which consists of feeding radioctive sodium phosphate and ascertaining the amount of radioactive phosphorus incorporated in the phosphatides.

PAGE, Indianapolis.

FUNCTIONAL LOCALIZATION IN THE CEREBELLUM OF PRIMATES. E. H. BOTTERELL and J. F. FULTON, J. Comp. Neurol. **69**:31 (Aug.) 1938.

For these studies, 18 specimens of Macaca mulatta and 3 of Papio papio were used. The cerebellar hemispheres were removed without injury to the pyramis, uvula or nodulus, or the posterior portion of the vermis was removed or divided in the mesial plane. Animals were allowed to recover; they were then examined and all activities watched for periods varying from nine to eleven days. Disturbances of posture and gait were recorded cinematographically in many instances. Detailed histologic examination of the cerebellum was carried out in 16 animals. Larsell's terminology of the cerebellum is followed in descriptions. Unilateral section of the cerebellar peduncles was followed by: (1) conspicuous ataxia of the ipsilateral extremities, with tremor and disturbances of equilibrium and gait; (2) transient ipsilateral hypotonia, more marked and enduring in the baboon than in the monkey; (3) progressive recovery, due to compensation from the other half of the cerebellum and in part from the frontal lobes; (4) nystagmus, which did not persist for more than twenty-four hours if the vestibular nucleus was undamaged.

In order to contrast the effects of unilateral section of all three peduncles with lesions restricted to structures in the midline, there was studied a group of animals in which the pyramis, uvula and nodulus were ablated and another group in which the cerebellum was split in the midsagittal plane. Serial sections were cut of all lesions. Lesions involving the pyramis, uvula and nodulus and the fastigial nuclei gave rise to equilibratory disturbance accompanied by relatively slight tremor and ataxia of the extremities. Complete longitudinal splitting also gave rise to serious and enduring disturbances of equilibration, as did damage to the globose, emboliform and dentate nuclei. The tremor was enduring if the dentate nuclei were extensively involved. No evidence was found of functional localization within discrete areas of the hemispheres. Botterell and Fulton conclude that the neocerebellum facilitates the execution of volitional movements, and its destruction in the macaque and baboon causes a syndrome of awkwardness, fatigability, slowness and hypotonia, accompanied by marked disturbances of motor progression.

ADDISON, Philadelphia.

REFLEXES IN THE SPINAL MONKEY. J. C. HINSEY and J. E. MARKEE, J. Comp. Neurol. **69**:471 (Dec.) 1938.

The spinal cords of 7 female Pithecus rhesus monkeys were transected between the tenth and the ninth thoracic segment. Each animal was examined over a period of thirty-four to one hundred and twenty days for knee and ankle jerks, plantar responses, ipsilateral flexion, the position support reflex, crossed flexion,

extension and adduction and rhythmic responses. At autopsy the levels and completeness of transections were verified. Plantar reflexes from plantar stimulation appeared first or simultaneously with the appearance of the knee jerk. The positive support reflex was not seen in any of the animals. Rhythmic reflexes were present, but were deficient. Crossed reflexes were poorly developed.

ADDISON, Philadelphia.

FACTORS LIMITING RECOVERY AFTER CENTRAL NERVOUS LESIONS. K. S. LASHLEY, J. Nerv. & Ment. Dis. **88**:733 (Dec.) 1938.

According to some authorities (von Monakow), the return of function after injury to the central nervous system is due to restoration of the anatomic substratum or its recovery from depression, and not to reorganization of neural pathways, while others (Franz, Foster) have expressed the belief that the functions of destroyed portions may be taken over by other structures not previously concerned. Theories concerning the mechanism of restitution vary from those postulating a spontaneous reorganization, independent of regeneration or reeducation, to those maintaining that every part of the nervous system participates in every function, so that recovery must involve complete reorganization of all that is left after a lesion. The problem is complex, since function may be lost through destruction, temporary cellular changes, diaschisis, metabolic disturbances or lowered tonic activity. Lashley confines his discussion to the problem of recovery following actual destruction of functioning mechanisms.

According to von Monakow's theory of diaschisis, the destruction of one region may cut off facilitating impulses to another center, which is thus rendered incapable of functioning. The available evidence fails to support this theory. Lashley thinks it more likely that in supposed cases of diaschisis some essential mechanism (such as the motor function of the arm) has been deranged, with resultant disturbance of a dependent function (such as the performance of discriminative acts), and that restoration of the basic process is followed by apparent restoration of the dependent function.

In some cases a destroyed function is immediately and apparently spontaneously superseded by an abnormal, but useful, adjustment. After interchanging the internal and external rectus muscles of the eye, Marina found all consensual reflex movements to be normal. Similarly, a new visual center of fixation may be developed in the eye, or a coordinated pattern of movements may be transferred from a monkey's paralyzed arm to its fellow of the opposite side. Such facts resemble the development of optic lobes and eyes from a piece of transplanted neural tube or the formation of a normal polyp from the pulverized tissues of a hydroid. Nerve tissue appears to reconstitute itself functionally in a fashion resembling the reconstitution of structure in regeneration.

The theory that one part of the brain may serve vicariously for a destroyed portion has never been well confirmed by experiment. Restitution of function by reeducation seems to depend on the preservation of some part of a limited system which is normally concerned in the same function. The premotor area can assume in part the functions of the destroyed precentral area, but when both are destroyed the paralysis is permanent. Similar restrictions apply to vicarious function in the visual system. The restitution of function can occur only within certain functionally interrelated zones, and the efficiency of cortical activity following injury appears to be dependent on the total mass of tissue available for any particular function.

Recent experimental work tends to show that the development of intelligence involves the addition of qualitatively, rather than quantitatively, different processes. Rats trained to choose the larger of two objects can "abstract" linear dimension, surface area or total illumination, but cannot be trained to select one of three unfamiliar objects which differs from the other two. This form of abstraction is easy for the monkey, while choosing an object to match a model is difficult for the lower monkey, possible for the chimpanzee and easy for man. Cerebral

lesions seem to act selectively on these different kinds of organization, and thus to lead to deterioration by a qualitative, rather than a quantitative, reduction of function. Lashley believes, however, that within each qualitative system there are quantitative variations, as measured by speed and consistency. These problems are well illustrated in the cerebral amnesias (aphasias). Such conditions generally affect classes of concepts rather than particular memories. Quantitative reduction of general capacity cannot explain these specific amnesias. On the other hand, a quantitative factor of general cortical activity, which Head termed "vigilance," seems to be a dynamic factor in recall. Reduction of this factor may retard or hamper reactions which are not actually lost. Every nerve function seems to depend both on a specific pattern of nervous organization and on the general level of nonspecific excitations constituting central tonus.

The role of reeducation in the restitution of function concerns only the specific patterns of activity, and not the general level of excitability. If the ability to abstract and to deal with complex situations is reduced, reeducation is ineffective except when the lesion occurs in early infancy. Restitution of function by education after lesions in infancy may be due to prevention of the normal regression of lower centers in such cases or to the building up of general capacities during the period of growth. Increased motivation or desire to recover, however stimulated, facilitates the recovery of functions, either by overcoming "functional" disorders superimposed on the organic or by increasing the irradiation of nerve impulses over new paths.

MACKAY, Chicago.

SOME OBSERVATIONS ON HEADACHE. D. W. C. NORTHFIELD, Brain **61**:133, 1938.

Headache as the initial symptom was present in 36 of 100 unselected cases of verified tumors of the brain. It was not the first symptom in 9 cases of acoustic neurinoma, but it was the initial symptom in 10 of 12 cases of tumors of the posterior fossa. The incidence of gliomas of the cerebral hemispheres was similar to that of cerebral meningiomas. Headache as the initial symptom was more common in cases of tumors of the temporal than of the frontal lobe. Headache is likely to precede other symptoms in cases in which the tumor, by reason of its location, tends to impede the flow of cerebrospinal fluid through the ventricular system. Of 121 cases, excluding those of pituitary adenomas, frontal headache was absent in only 5 per cent, as compared with 25 per cent in which the tumor was infratentorial. Pain in the neck was present in 22 per cent of cases of supratentorial tumors and in 49 per cent of cases of infratentorial tumors. The headache was entirely or predominantly unilateral in 42 cases and did not shift from side to side. In 6 of these cases the tumor was situated approximately in the middle line, but in only 4 cases was the tumor on the side opposite that of the headache.

It is commonly accepted that the headache produced by an intracranial tumor is due to increase in intracranial tension. Of a series of 102 verified cases of tumor of the brain, the pressure exceeded the normal in 63; in 39 it was less than 200 mm. of fluid, and in 16 it was below 100 mm. In many cases in which the pressure was normal or subnormal there was severe headache. In many patients headache may be absent although the intracranial pressure is very high. These cases demonstrate that the absolute value of the intracranial pressure bears no relation to the presence or absence of headache. Although headache is clearly related to diseases which produce an increase in intracranial pressure, the high pressure in itself is probably not the cause of the pain.

Certain conditions other than intracranial tumor suggest the possibility that headache may be vascular in origin. Patients suffering from an intracranial aneurysm often complain of recurrent headache, which commonly affects one side of the forehead more than the other. This suggests that the gradual stretching of the wall of the artery and the final rupture of the aneurysm may set up a train of afferent stimuli which is interpreted as headache.

During operative procedures, observations were made to determine the relative sensitiveness of various tissues. In the majority of cases the traction necessary to produce pain on stimulation of the dura mater was considerable. The tentorium seemed to be more sensitive than other areas of the dura mater, except that around the middle meningeal arteries; the dura mater lining the vault was the least sensitive. Pressure on or displacement of the internal carotid artery in the vicinity of the anterior clinoid process resulted in pain in or near the homolateral eye in 3 cases, pain in the homolateral temple in 1 case and no sensation in 1 case. In no case did sensation of any kind result from pressure on the pia mater, the brain tissue or the walls of the ventricles. The cortical veins and arteries and the choroid plexus were insensitive to clamping and to endothermy.

The effect of raising the intraventricular pressure was noted in 4 cases. Warm Ringer's solution was injected quickly into the ventricles in the course of ventriculographic examination, before the removal of any cerebrospinal fluid. Headache resulted in 2 cases. In 3 cases of tumor high in the spinal cord Ringer's solution was injected into the cisterna magna. In 1 case, after the injection of only a few cubic centimeters of fluid the patient complained of severe frontal headache. Twenty cubic centimeters of Ringer's solution injected under the dura mater in the course of cerebellar exploration, probably into the subdural space, has resulted in homolateral occipital headache, which gradually disappeared as the fluid escaped. Compression of the jugular veins for two minutes induced headache in 6 of 9 cases, and in 4 of these the resulting intracranial pressure was not above 200 mm. of water.

In many cases headache was produced by suddenly reducing the intracranial pressure. In 5 cases in which the lateral ventricles were tapped the sudden escape of fluid was attended by considerable pain.

Headache does not occur during the ventriculographic procedure, whereas it is intense during encephalographic examination.

From study of clinical material and experimental observations it appears that the sudden increase or decrease of pressure, previously normal or abnormal, readily causes headache. Rapid reduction of pressure is perhaps the more conspicuously successful method. The conclusion may be drawn that it is the sudden variation in the intracranial pressure, and not the steady pressure itself, which induces experimental headache.

Histamine phosphate was injected into 14 patients suffering from tumor of the brain, and in 11 cases the headache which occurred was similar in quality and distribution to that produced by the tumor. During the course of cerebral arteriographic examination histamine phosphate was injected into the common carotid artery in 13 patients, resulting in homolateral headache in 6 cases and bilateral headache in the others, the headache being more severe on the homolateral side. The injection of histamine in the internal carotid artery resulted in homolateral headache in all of 5 cases. In the same 5 cases, injections into the external carotid artery did not produce headache. Division of the middle meningeal vessels did not prevent bilateral headache following the intravenous injection of histamine.

The only intracranial tissue other than the dura mater which is sensitive to suitable stimuli is apparently the cerebral blood vessels. It is Northfield's belief that the headache associated with intracranial tumor is due to disturbance of the tension of the walls of the cerebral vessels. It is this disturbance which provides the adequate stimulus for the excitation of pain. SALL, Philadelphia.

EXPERIMENTAL DIABETES INSIPIDUS. J. H. BIGGART and G. L. ALEXANDER, J. Path. & Bact. **48**:405 (March) 1939.

In an attempt to arrive at some conclusion as to the factor or factors responsible for the production of diabetes insipidus, experiments on the dog were begun by Biggart and Alexander about three years ago. They found it possible to produce diabetes insipidus in dogs (temporary polyuria in 15 animals and permanent polyuria in 14) by a lesion which involves the supraoptic nuclei or the supraoptic hypophysial

tracts. It appears that the hypothalamus and the complex of the posterior lobe of the hypophysis must be considered a functional unit as regards water metabolism; the experiments suggest that the supraoptic hypophysial tract serves as the motor-secretory mechanism for the elaboration of the antidiuretic factor. In other words, even when the lesion in a patient with diabetes insipidus is confined to the hypothalamus, the syndrome is in effect an endocrine deficiency, due to the lack of stimulus for the secretion of the hormone. It is probable that there exists a quantitative relationship between the amount of damage done to the supraoptic hypophysial tracts and the polyuria, as in the present experiments unilateral damage did not result in permanent polyuria. The three phases which were seen during the onset of permanent experimental polyuria were transient polyuria, a period of normal output and, finally, appearance of the permanent phase. Hypophysectomy or pancreatectomy abolished this polyuria, while thyroid medication usually increased it. The authors conclude that the supraoptic nuclei are in some way sensitive to the water needs of the body, that they serve as the nerve centers which stimulate the secretion of the antidiuretic factor and that this factor is in all probability manufactured in the pars nervosa. Diabetes insipidus results when this neuroendocrine system loses its functional integrity, by reason either of a hypothalamic lesion interrupting the path of motor-secretory impulses or of replacement or destruction of the secretory tissue in the pars nervosa. In order that such loss of functional integrity may be clinically apparent, a certain amount of functioning tissue in the anterior lobe hypophysis must be present. This diuretic function of the anterior lobe is probably mediated through other endocrine glands, and the evidence available suggests that the thyroid and pancreas are of importance in this respect.

J. A. M. A.

Rolling Movements in Pigeons. E. Huizinga, Arch. f. d. ges. Physiol. **240**: 713, 1938.

Huizinga studied the rotation of the head appearing in pigeons several days after unilateral labyrinthectomy. If first one labyrinth is extirpated and the second labyrinth is removed after several months, the deficiency symptoms are much more marked than after the first labyrinthectomy; rotation of the head appears within twelve hours. These phenomena suggest the importance of the compensatory process in the vestibular nuclei in the genesis of the rotation. Rolling movements appeared in 1 animal. They are due to the marked rotation of the head, which finds no support.

Spiegel, Philadelphia.

Disturbances of Carbohydrate Metabolism of Cerebral Origin. S. Lups, Ztschr. f. d. ges. Neurol. u. Psychiat. **164**:644 (Feb.) 1939.

Lups reports 2 cases of diencephalic symptoms and disorders of carbohydrate metabolism. The first was a case of migraine with transitory changes in the blood sugar suggesting diabetes mellitus. During the attacks of hemicrania the blood sugar level dropped below normal. The author considers migraine a disturbance of the diencephalon. The second case was that of a man with psychopathic tendencies who had suffered from polydipsia since childhood and from frequent fluctuations in weight which were not in reaction to any evident circumstance. A disturbance in carbohydrate metabolism was discovered. The association of the disorders in carbohydrate metabolism with other diencephalic symptoms is in favor of the existence of a mechanism in the diencephalon regulating carbohydrate metabolism.

Savitsky, New York.

Pain and Muscular Fatigue. S. W. Golmann, Acta med. U.R.S.S. **1**:45, 1938.

Golmann discusses the problem of muscular fatigue in patients with nerve lesions when there is a sensation that the paralyzed or lost extremity is doing muscular work. The feeling of fatigue in the severed or lost extremity is followed

by a sensation of extreme fatigue and then of pain if the illusion of work persists. This is occasionally accompanied by a feeling of warmth, flushing of the face, rapid breathing and tachycardia. The author states that in actual work the fatigue is essentially a thalamic phenomenon. In illusory or fancied work the feeling of fatigue appears even more quickly than in a healthy extremity, owing to the fact that the sensory threshold is lowered in the thalamus because of release of peripheral control. Golmann discusses also the question of fatigue in cases of hyperkinesis associated with diseases of the extrapyramidal system. In a case of parkinsonism with constant bending and unbending of the knee, even against a load of from 14 to 16 Kg., there was no feeling of fatigue. The author explains this by the fact that in encephalitic parkinsonism there is involvement of the basal ganglia, so that feelings of fatigue and pain do not arise.

Fatigue accompanied by pain is due to increased excitability of the optic thalamus, which in turn transmits impulses to the hypothalamus, producing changes in temperature and metabolism. In the hypermotility of parkinsonism there is no fatigue, owing to a heightened threshold of excitability of the optic thalamus.

KASANIN, San Francisco.

FUNCTIONAL CONNECTION OF THE CEREBRAL CORTEX WITH THE VISCERA. C. M. BYKOV, Acta med. U.R.S.S. **1**:178, 1938.

Bykov states that it is easy to obtain conditioned reflexes from visceral organs. In all experiments, however, after nine or ten stimulations, during which the reflex is established, the response disappears if no reenforcement is used. The author describes conditioned reflexes of the kidney, liver and spleen. The spleen in a dog was transplanted under the peritoneum of the abdomen, where it could be easily felt. Slight stimulation of the muscles of the hindlegs caused contraction of the muscles and increase in the volume of the spleen, which was recorded with an oncograph. Stimulation of the hindleg was associated with a loud whistle. After a while one could obtain increase in the volume of the spleen merely through the sound of the whistle. The same experiments were conducted with the duodenum and intestine. The author tried to establish the relationship of the vegetative nervous system to the cortex. The basal metabolic rate was studied in a group of patients who were engaged in a rhythmic exercise. The rhythm of the motions was established through metronome beats. After several sessions, changes of metabolism were obtained after beating of the metronome alone. Bykov states that the cortex influences not only the visceral organs but also the tissues and all intracellular processes. He believes that the cortical impulses are transmitted by humoral agents.

KASANIN, San Francisco.

Neuropathology

PITUITARY FIBROSIS WITH MYXEDEMA. BENJAMIN CASTLEMAN and SAUL HERTZ, Arch. Path. **27**:69 (Jan.) 1939.

Castleman and Hertz report a case of destruction fibrosis of the anterior lobe of the pituitary gland without cachexia. On the contrary, the patient not only was in a good state of nutrition but had myxedema. At necropsy, fibrosis of the anterior lobe of the pituitary and atrophy of the thyroid, parathyroids, adrenal glands, ovary and uterus were observed. The authors present pathologic and experimental evidence purporting "to establish the primacy of the anterior lobe of the pituitary in the pathogenesis of the disease." From the microscopic observations alone the diagnosis in this case would be Simmond's disease, but the absence of cachexia raises the question whether the cases in which there is no cachexia represent a special disease group. Pluriglandular insufficiency would probably be a more accurate clinical designation. The lesion in the pituitary gland was that of destruction of "most of the cells of the anterior lobe," plus lymphocytic infiltration. The lesion in the thyroid was devoid of inflammatory elements.

Castleman and Hertz conclude that in their case the primary disease was in the pituitary and that atrophy of the other endocrine glands was secondary. This is borne out by the fact that with primary destruction of the thyroid the anterior lobe of the pituitary is often hypertrophied. In rats, after hypophysectomy, the thyroid, parathyroids, ovary and adrenal glands undergo atrophy. This is in complete harmony with the changes in the case reported.

WINKELMAN, Philadelphia.

POSTMEASLES ENCEPHALITIS. JOSEPH ZISKIND and HERBERT J. SCHATTENBERG, Arch. Path. **27**:128 (Jan.) 1939.

Ziskind and Schattenberg report a case of postmeasles encephalitis in which the patient lived for eight months after the attack of measles. The most prominent microscopic feature was the perivascular proliferation of microglia elements, with scattered hematogenous elements in the perivascular spaces, these were mainly lymphocytes, with occasional plasma cells. Perivascular demyelination, with the presence of fat-containing glia cells, was another common feature. In addition, there was swelling or hyperplasia of the vascular endothelium.

WINKELMAN, Philadelphia.

PATHOLOGIC ASPECTS OF POSTERIOR PROTRUSIONS OF THE INTERVERTEBRAL DISKS. WALTER G. DEUCHER and J. GRAFTON LOVE, Arch. Path. **27**:201 (Feb.) 1939.

Deucher and Love report a microscopic study of 100 intervertebral disks removed because of neurologic or orthopedic indications. The disks were composed of all parts normally present in the unprotruded disks: the annulus lamellosus, including its outer parts, and the nucleus pulposus, with occasional remnants of the notochord. The tissue of the intervertebral disk was almost invariably altered in the protrusion. The most common and constant changes consisted of alterations of the normal architecture. Degenerative changes, too, were seen commonly. Advanced degeneration was more frequent among patients in the older age groups. Marked degeneration of the cartilage cells was much more common than degeneration of the fibrils. Fibrosis was observed to occur in the form of proliferating fibrous tissue or in close relation to remnants of the notochord. In both instances the fibrous tissue tended to replace the normal fibrocartilaginous structures of the protruded portion of the disk. Edema of the protruded part of the intervertebral disk was an important and frequent observation. It involved the annulus and the nucleus pulposus, and was more frequent in young persons. The edema of the protrusion must be considered as a result of the capacity of the nucleus to swell if the normal forces keeping it in place and shape are decreased. At the same time it may be helped or held back by circulatory changes resulting from the displacement of the protruded part. The occurrence of edema may result in exacerbation of the clinical symptoms. Such an exacerbation, however, may subside spontaneously or with conservative treatment.

It was not possible from this study to draw any conclusions about an etiologic relationship of notochordal rests to protrusions of the intervertebral disks.

WINKELMAN, Philadelphia.

PATHOLOGIC CHANGES IN THE NERVOUS SYSTEM IN YELLOW FEVER. LEWIS D. STEVENSON, Arch. Path. **27**:249 (Feb.) 1939.

Stevenson reports on the changes in the brain in 20 cases of yellow fever. Perivascular hemorrhages were found to be the most important lesion in the nervous system. The hemorrhages were most frequent in the subthalamic and periventricular regions, at the level of the mamillary bodies. Next in order of involvement were the temporal pole and the cerebellum. Slight perivascular lymphocytic exudate was noted in 9 cases. Changes in the nerve cells were

insignificant, and no inclusion bodies were seen. Reactive changes in the microglia and astrocytes were slight. Stevenson concludes that there was no definite evidence of neurotropism on the part of the virus of yellow fever in his series of cases.

WINKELMAN, Philadelphia.

GLIOMATOSIS CEREBRI. SAMUEL NEVIN, Brain **61**:170, 1938.

Scattered reports of cases characterized pathologically by diffuse cellular overgrowth throughout the cerebral hemispheres have appeared in the literature. Landau (Diffuse Glioma of the Brain, *Frankfurt. Ztschr. f. Path.* **5**:469, 1910) described the case of a man aged 29 who died suddenly after intermittent headaches and epileptic attacks for three years. Autopsy revealed diffuse enlargement of the anterior part of the right cerebral hemisphere. Microscopic examination revealed widespread but variable gliomatous degeneration of the cortex and thalamus on the left side. Landau called the cells undifferentiated glia cells and the condition a diffuse glioma which had arisen at different points in a congenitally abnormal tissue and had spread by continual involvement of other regions in the pathologic process.

Nevin reports 3 cases in which there were similar pathologic features. The first case was characterized clinically by symptoms of gradually increasing intracranial pressure, associated with general mental dulness, marked failure of memory and epileptic attacks. The pathologic process consisted of a new growth of spongioblasts and astrocytes, irregular and variable in shape, size and form, throughout wide areas of the cerebral cortex, basal ganglia, thalamus and upper part of the brain stem. This new growth was implanted in the normal structure of the nervous system and produced comparatively slight secondary changes in the essential nerve elements. The cells were spongioblasts and astrocytes in irregular arrangement, and the fiber formation was a coarse, wide open network. The subcortical zone of the white matter was more affected than the deeper parts of the white matter, and here the growth was mainly astrocytic, with a dense, fine glial network. In the thalamus there was a spongioblastic and astrocytic growth with dense fiber formation. The second case was characterized clinically by a history of epilepsy throughout life and mental deterioration, failure of memory and changes in character for four years. Death followed the development of symptoms of increased intracranial pressure and right hemiplegia. The pathologic process consisted of a new growth of spongioblasts and astrocytes throughout wide areas of the anterior parts of the cerebral hemispheres, especially on the left side, and involving also the brain stem. This new cell formation was superimposed on the essential nerve elements, producing in these structures severe secondary changes in the areas of greatest growth. It was accompanied by varying gliosis. In the white matter this was a fine, dense network, arising from small astrocytic cells, whereas in the gray matter the glial increase was a coarse, open network, formed for the most part by the processes of large astrocytic and spongioblastic cells, except along the small blood vessels, where bundles of fine fibers were also present. There were an anaplastic focus of true tumor formation in the midst of the general cellular overgrowth and a neurofibroma in the suprapituitary region. The third case was characterized clinically by epilepsy, failure of memory and symptoms of increased intracranial pressure. Pathologically, there was diffuse cellular overgrowth throughout wide areas of the anterior parts of the cerebral hemispheres. This was formed of astrocytic and spongioblastic cells and was superimposed on the essential nerve structures. The accompanying gliosis was not entirely irregular, but was greater subpially and in the white matter and less in the gray matter.

These cases cannot be regarded as examples of tumor. The retention of the normal elements of the nervous system, even in areas of severe new cell formation, is much greater than is seen in true tumors of the nervous system. It would be impossible to designate as a tumor formation by direct spread an overgrowth in which the cellular and fiber hyperplasia varies. This feature seems to indicate

that the new-formed cells had not escaped entirely from the laws that govern normal growth and that to a much greater extent than is usual in simple tumor formation their development was influenced by the normal structures in which the overgrowth was taking place.

In the brain stem and in the cortical areas not involved in the general cellular overgrowth there were abnormalities in the neuroglia which cannot be regarded as a direct spread of tumor tissue throughout the nervous system. This probably indicates a developmental abnormality of the neuroglia in general. The pathologic process has therefore been regarded not as a neoplasm in the strict sense of the term but as a blastomatous malformation, in some way congenitally predetermined.

SALL, Philadelphia.

SUBACUTE DIFFUSE EPENDYMITIS. R. M. STEWART, Brain **61**:192, 1938.

It is possible to recognize three forms of ependymitis, acute, subacute and chronic. The first is comparatively common, in most cases being either merely the extension of purulent meningitis to the ventricles of the brain or, as in meningococcic meningitis, part of a septicemia in which the organisms reach the ventriculosubarachnoid system not by way of the meninges but through the choroid plexus. Chronic ependymitis is of an altogether different character. For example, the so-called granular ependymitis characteristic of parenchymatous syphilis owes its development to subependymal glial overgrowth rather than to actual hyperplasia of the ependymal lining, and its presence is only one indication of a widespread proliferative gliosis which spares no part of the nervous system. Subacute ependymitis differs from the other two forms in that it is capable of arising as an isolated and primary inflammation of the entire ventricular system, limited strictly to this system, with no concomitant inflammation in the subarachnoid space.

Stewart reports the case of a feebleminded woman aged 56 years who succumbed to bacterial endocarditis, of eighteen months' duration. Clinically, the patient had presented vague neurologic signs, of no localizing value. Necropsy revealed the presence of subacute ependymitis of the lateral, third and fourth ventricles; associated with this was partial stenosis of the aqueduct of Sylvius, which had produced a marked degree of internal hydrocephalus. Inflammatory changes were limited to the ependymal and subependymal regions of the brain, and, except for the presence of leptomeningitis in the upper cervical region of the cord, the pia-arachnoid was free from evidence of inflammation. Large numbers of micro-organisms were present among inflammatory cells lying on the surface of the ependymal lining of the ventricles. Marked proliferation of the subependymal glia accompanied these changes.

In the absence of any widespread inflammatory reaction, in either the cerebral cortex or its membranes, it is evident that the case reported is an example of the relatively uncommon form of ependymitis for which the term "primary" is justifiably employed. In this type the inflammatory process is limited strictly to the ependymal lining of the intraventricular system of the brain, and the symptoms to which it gives rise are largely those of obstructive hydrocephalus secondary to closure of the ventricular foramens. Little is known with regard to the etiology in these cases.

SALL, Philadelphia.

CEREBRAL CORTICAL MYELINOPATHY IN CARBON MONOXIDE POISONING. Y. K. HSÜ and Y. L. CH'ENG, Brain **61**:384 (Dec.) 1938.

Hsü and Ch'eng made postmortem examinations in 3 cases of carbon monoxide poisoning. In 1 of these there was typical bilateral hemorrhagic softening in the globus pallidus, with no significant changes in the white matter, and in 2 diffuse changes occurred in the deeper cerebral white substance. Clinically, the disease in these 2 cases was of the so-called relapsing type; that is, secondary changes appeared after recovery from the initial disturbances. One of these patients presented symptoms of catatonia and parkinsonism and died four months after the

poisoning. In the other patient bronchopneumonia and empyema developed, and he died four weeks later. Both brains showed more or less diffuse degeneration of the white matter, with progressive changes of glia cells and patches of demyelination. There was no bilateral softening of the globus pallidus. A direct influence of the poison, or its anoxemic effect on the nerve tissue, is emphasized as a prominent pathogenic factor in these cases.

J. A. M. A.

Psychiatry and Psychopathology

ASSOCIATION OF STAMMERING AND THE ALLERGIC DIATHESIS. A. M. KENNEDY and D. A. WILLIAMS, Brit. M. J. **2**:1306 (Dec. 24) 1938.

Kennedy and Williams examined a consecutive series of 100 children who stammered. These children were from 5 to 14 years of age. Of the children examined, 81 were boys and 19 girls; 89 proved to be right handed and 11 left handed, and a family history of stammering was present in 65 cases and absent in 35. Fifty-two children gave a personal history of allergic manifestations: Migraine plus urticaria and/or asthma was complained of by 32; 11 complained of urticaria alone; 8 had a history of asthma plus eczema and/or hay fever, and 1 suffered only from eczema. Thirty of these 52 children also gave a history of "fastidiousness" with regard to food generally and dislikes or refusals of particular foods or gastrointestinal upsets after them. Of these 52 children with a personal history of allergy, 48 also had a family history of allergy. In 37 cases one or both parents exhibited allergic manifestations, and in 6 a grandparent was the nearest sufferer. An aunt was the nearest relative in 4 cases, and the allergic symptoms were observed in a sister of the child in 1 case. Thirty-three of the 52 children (including the 4 with no allergic family history) had a family history of stammering. Seven of the 52 children were left handed; 6 of these 7 had a family history of allergy and 2 also a family history of stammering. Of the 48 children who gave no personal history of allergic manifestations, all but 1 had a family history of allergy. Fifteen of these children, however, gave a history of "fastidiousness" with regard to food generally and dislikes or refusals of particular foods or gastrointestinal upsets after them. Thirty-seven of these 47 children had one or two parents who suffered from allergy; 5, a grandparent; 2, an aunt, and 3, a sister. Thirty-two of the 48 children (including the one with no allergic family history) had a family history of stammering. Four of the 48 children were left handed, and all had an allergic family history. Three also had a family history of stammering. The close and practically constant association of stammering and allergic manifestations in the personal and family histories of the stammerer, as revealed by the present investigation, favors the view that there is something more than a casual relationship between stammering and the allergic diathesis.

J. A. M. A.

THE ELECTRO-ENCEPHALOGRAM IN SCHIZOPHRENIA. J. F. MACMAHON, J. Ment. Sc. **84**:78 (Sept.) 1938.

The electroencephalograms of 30 schizophrenic patients were recorded with a portable two channel apparatus. Eye movements and blinking were found to produce artefacts which made interpretation of some results difficult and threw doubt on the value of Hoagland's "delta index" as a measure of the degree of abnormal activity. A certain number of patients displayed a true delta discharge, which had no fixed focus but was most marked in the frontal lobes of the more stuporous patients. The delta discharge vanished in 2 patients under metrazol therapy and in 1 patient with spontaneous remission. Two cases were described in which a persistent alpha rhythm was associated with a psychosis featuring volitional weakness. Two types of electrical abnormality occur in schizophrenia: first, a variation within the physiologic range, that is, unusual persistence and prominence of the normal alpha rhythm involving chiefly the postcentral regions,

and, second, a truly pathologic delta discharge most marked in the frontal lobes, not in one area only but intermittently in many places. Neither of these abnormalities is diagnostic of schizophrenia, nor do they throw much light on the pathogenesis of the disease.

KASANIN, San Francisco.

IMAGERY AND ITS RELATIONS TO SCHIZOPHRENIC SYMPTOMS. LOUIS H. COHEN, J. Ment. Sc. **84**:284 (March) 1938.

Twenty-one schizophrenic patients were tested with reference to their imagery by the use of "test A," published in the appendix to C. H. Griffitts book (Fundamentals of Vocational Psychology, New York, the Macmillan Company, 1924, p. 372). Cohen concludes from the data collected that the total clinical picture in schizophrenia is the result of one of two processes, active and passive. The nature of the schizophrenic process in patients of these respective groups is differentiated by the direction of the preponderating imagery. In both groups there is preoccupation of the patient with imagery intimately relating to his body, but in one group (kinesthetic) the imagery has an outward direction and in the other (tactual-temperature and/or olfactory-gustatory) it has an inward direction. In the first group the form of the symptoms represents projection toward the outer world; in the second group there is projection toward the inner world of the body. It is not yet possible to establish proof that one or the other direction is to be considered more malignant or benign. The importance of the present observations seems to be that the direction of the changed imagery determines to a large extent, if not exclusively, the form, if not the production, of specific symptom pictures.

KASANIN, San Francisco.

STUDIES IN HAY-FEVER PATIENTS (THE ALLERGIC PERSONALITY). ERICH WITTKOWER, J. Ment. Sc. **84**:352 (March) 1938.

Fifty hay fever patients and 50 patients with fractures or acute appendicitis were submitted to a psychologic examination for purposes of comparison. The personality structure prevailing among hay fever patients was found to be characterized by self absorption, dreaminess and overweening ambition.

KASANIN, San Francisco.

THE RANGE OF MENTAL REACTION STATES INFLUENCED BY CARDIAZOL CONVULSIONS. L. C. COOK, J. Ment. Sc. **84**:664 (Sept.) 1938.

Cook bases his conclusions on 130 completed courses of convulsive therapy given for a wide variety of conditions. Convulsive therapy selects neither particular mental diseases nor individual symptoms, but influences a number of morbid reaction types. It seems to matter less in what mental disorders the morbid reaction states occur than how deeply rooted they are and how much dissociation accompanies them. This may help to explain why stupor is more easily influenced than hebephrenia or simple schizophrenia, which are usually associated with more comprehensive dissociation. In the same way, paraphrenic states without much affective or conduct change are especially intractable. Recurrent conditions, whether schizophrenic or not, seldom show gross dissociation and therefore tend to respond well. In nearly all cases abstraction from reality is broken, in some patients with an early form dramatically and completely, in others gradually and perhaps by stages, while in some subjects with chronic disease it is influenced to an extent only sufficient to produce a free outlet of previously hidden psychotic symptoms. Delusions and hallucinations are eradicated only when the schizoid personality and deranged affective state can be modified. When delusional symptoms have become almost a habit and there is little affective abnormality, metrazol is of no value. In depressive reactions, whatever their type, and in states of excitement and elation the same response is seen. As the affective morbidity disappears, the psychotic ideas and behavior evaporate. Similarly, hysterical symptoms, hypochondriacal ideas and anxiety features are lost only as a consequence of change of outlook.

KASANIN, San Francisco.

CONSANGUINITY AND MENTAL DISORDER. T. A. MUNRO, J. Ment. Sc. **84**:708 (Sept.) 1938.

Munro made an inquiry into the incidence of consanguineous parentage among the populations of hospitals for mental disease in seven English counties and in two cities, Cardiff, Wales, and Edinburgh, Scotland. The inquiry also included the examination of 152 patients with related parents and the comparison of them and of their families with a similar group of patients with unrelated parents selected at random from the populations of hospitals for mental disease.

Munro concludes that there exists a definite and specific familial incidence of mental disease. The relatives of patients with affective psychoses, when they are psychotic, tend to suffer from affective psychoses, and the relatives of schizophrenic patients suffer from schizophrenia. This specific familial incidence is true not only for the broad reaction types but also for each clinical type within the group, except for the organic psychoses of exogenous origin. The more strict the criterion of manic-depressive disease in the patient, the more typically manic-depressive are the disordered relatives and the more definitely dominant is the inheritance. Familial incidence holds for the schizophrenias; it is most evident in the paranoid form and least evident in the catatonic form. The incidence of mental disorder among relatives decreases in an orderly way with the decreasing degree of relationship to the patient. KASANIN, San Francisco.

VITAMIN C DEFICIENCY IN ACUTE MENTAL DISORDER. F. T. THORPE, J. Ment. Sc. **84**:788 (Sept.) 1938.

Thorpe investigated the incidence of vitamin C deficiency in a hospital for mental disease by estimating the daily excretion of ascorbic acid in the urine and the urinary response one hour after an intravenous test dose of 500 mg. of ascorbic acid. Of 58 patients examined, 39 (67 per cent) were found to excrete less than the minimum normal standard of 20 mg. daily. In 22 cases the daily excretion was below 15 mg. Deficiencies were more prevalent among the women patients. In response to the test dose of ascorbic acid, 14 of 38 patients gave indications of varying degrees of vitamin C deficiency. Such deficiency can usually be demonstrated in the toxic confusional psychoses, particularly in cases of puerperal disorders. Lesser degrees of deficiency are found in melancholic and senile states. There is no evidence of any direct causal relation between vitamin C deficiency and mental disorder; when a deficiency is found it is usually part of general malnutrition. In these cases administration of the vitamin frequently plays an important part in bringing about the mental, as well as the physical, recovery of the patient. KASANIN, San Francisco.

REMISSIONS IN SCHIZOPHRENIA: INSULIN AND CONVULSION THERAPIES COMPARED WITH ORDINARY TREATMENT. H. STALKER, W. M. MILLAR and J. M. JACOBS, Lancet **1**:437 (Feb. 25) 1939.

Stalker and his colleagues compare the results obtained in the treatment of 218 patients with schizophrenia, divided into three series according to whether treatment was by ordinary hospital methods, with hypoglycemia or with convulsant drugs. There was no significant difference in the numerical results obtained in treatment of schizophrenia by the three methods. Spontaneous remissions occurred most often in acute schizophrenic illnesses which could not be fitted into the standard subgroups and in cases in which the affect was well preserved and there was little or no disharmony between mood and thought. Hypoglycemia gave the best results in cases of the paranoid subgroup and in those in which the affect was well preserved. There were no important complications. Convulsion therapy appeared to be best suited to stupor reactions. It was also useful in cases of psychoneurosis resistant to psychotherapy. The disadvantages of the treatment are that about half the patients object to it and that injuries may occur. Occasionally patients were made worse mentally. The field of special therapy is limited, but each method

should be used in treatment of the special type indicated. It affords the best chance of recovery to a potentially recoverable patient whose illness is dragging on. It reduces the average duration of hospital treatment. J. A. M. A.

DURATION OF SPONTANEOUS REMISSIONS OF SCHIZOPHRENIC PSYCHOSES: WHAT CAN BE ATTAINED WITH THE SHOCK THERAPY? G. LANGFELDT, Ztschr. f. d. ges. Neurol. u. Psychiat. **164**:494 (Jan. 23) 1939.

Langfeldt deplores that many investigators of the shock therapy of schizophrenia overlook the fact that their statistical reports are of limited value as long as they fail to state what forms of schizophrenia were treated. He shows that the psychoses, which are designated as schizophrenia, can be divided into two main groups: (1) the typical schizophrenias, that is, the conditions which in Kraepelin's terminology are designated as dementia praecox, and (2) the so-called schizophrenias, the "schizophreniform psychoses." The second group includes chiefly manic-depressive aspects and psychopathic tendencies (paranoid, hysterical, asthenic, cyclothymic, schizoid and others). The typical and the atypical schizophrenias differ greatly as to their prognosis. The atypical schizophrenias are nearly all spontaneously cured, and, except in a few cases in which the course is intermittent, the cure is permanent. Shock therapy shortens the duration of the atypical psychoses. However, it cannot be definitely said as yet whether this is a permanent advantage. Among the schizophreniform conditions that have an acute onset are those in which the typical schizophrenic symptomatology is shown. If these conditions are not treated the prognosis is unfavorable. However, it will require further investigations to determine whether these forms are amenable to shock therapy. The author says that there is an increase in reports which show that the atypical schizophrenias are the ones that react favorably to shock therapy with insulin or metrazol. He emphasizes that all reports on shock therapy of schizophrenia should give attention to the differentiation between typical and atypical forms of schizophrenia. J. A. M. A.

Meninges and Blood Vessels

MENINGITIS DUE TO STAPHYLOCOCCUS AUREUS HAEMOLYTICUS. MILO FRITZ and WILLIAM HOLLISTER, Arch. Otolaryng. **27**:317 (March) 1938.

Only 4 cases of recovery from meningitis due to Staphylococcus aureus haemolyticus have so far been reported in the literature. In the cases reported by Stout, Shless and Dunlap the patients recovered after the administration of Staph. aureus bacteriophage. Fritz and Hollister consider their case unique in that it is the first reported in which recovery followed the use of staphylococcus antitoxin. A white boy aged 13 gave a history of a cold twelve days before admission. Five days later there developed pain in the right ear, with chills and fever. A tender swelling over the right temporal region then developed and paracentesis of the right ear drum was followed by free discharge of yellow pus. Two days later the drainage ceased; pain increased, and the temporal swelling extended to the mastoid region. Two hours after the patient was first seen by the authors mastoidectomy was performed on the right, with the patient under general anesthesia. The lateral sinus was not involved, and the dura appeared healthy. The pus showed Staph aureus haemolyticus. The first two days after operation were uneventful. On the evening of the third day the patient became drowsy, and headache developed, with rise in temperature. The left ear drum appeared normal, but it was incised and fluid was obtained. Neurologic examination gave normal results up to this point, except for the presence of spontaneous nystagmus, which had been present since birth. A roentgenogram showed that the left mastoid was involved. The petrous region was clear on both sides. Chills again appeared on the fifth day, with the temperature up to 106 F. The left mastoid was operated

on, and thick yellow pus was seen. The dura and lateral sinus were explored and observed to be normal. The same day the patient became totally deaf, drowsy and rigid and began to vomit. Lumbar puncture showed 24,000 cells; a culture of the fluid yielded Staph. aureus haemolyticus; 10,000 units of staphylococcus antitoxin was injected intraspinally after the cutaneous and conjunctival tests gave negative results. Prontosil (the disodium salt of 4-sulfamidophenyl-2-azo-7'-acetylamino-1'-hydroxynaphthalene-3', 6'-disulfonic acid; now known as neoprontosil) was injected intramuscularly every four hours. The patient was given a transfusion. A second culture was positive for the staphylococcus, after which the cultures were sterile and the patient improved rapidly. One month later the patient still had pus in both ears and was completely deaf to everything but the loudest tones. Staphylococcus antitoxin and transfusion were credited with being the important factors in recovery; prontosil may have been an accessory factor.

HUNTER, Philadelphia.

RELATION OF THE INTERNAL EAR SPACES TO THE MENINGES. H. B. PERLMAN and J. R. LINDSAY, Arch. Otolaryng. **29**:12 (Jan.) 1939.

The pathways by which infection may spread from the temporal bone to the meninges and the relation of labyrinthine infection to middle ear suppuration and infection within the subarachnoid space are important to otologists on account of the frequency with which meningitis follows otitic disease. Fifty-eight temporal bones from 30 patients who died of meningitis in the acute stages were studied. The earliest manifestation of invasion of the labyrinth consists of a collection of inflammatory cells in the subarachnoid space about the seventh and eighth cranial nerves in the internal acoustic meatus, without destruction of the arachnoid. A demonstrable subarachnoid space can usually be treated to the mouth of the foramen for the facial nerve in the internal acoustic meatus, sometimes as far as the geniculate ganglion and rarely beyond it, and pus cells in the subarachnoid space about the facial nerve in this area can be observed. Usually, just beyond the foramen the pia-arachnoid becomes closely applied to the trunk of the facial nerve to form its perineurium, effecting a barrier to pus cells extending along the facial canal in the early stages of infection. There is a similar distribution of the arachnoid about the branches of the eighth nerve. At the foramens in the internal auditory meatus the arachnoid and the dura unite, obliterating the subdural and subarachnoid spaces. In the early stages of meningitis the fluid in the perilymphatic spaces exhibits an increased affinity for the eosin stain, which indicates that early chemical changes have taken place. This reaction makes its appearance first in the scala tympani adjacent to the round window, and in later stages involves the perilymphatic spaces more generally, at which time they stand out in contrast to the endolymphatic spaces. Next come invasion of the cochlear aqueduct and the appearance of pus cells about its opening into the scala tympani, without destruction of the arachnoid meshwork in the aqueduct. In a short time pus cells invade further and extend along the various branches of the nerves and vessels, eventually reaching the perilymphatic space. Next there are found pus cells in the perilymphatic spaces. Adhesions develop; the dura may become thickened, and edema may paralyze the facial nerve. Every specimen examined, regardless of the duration of the disease, showed pathologic evidence of meningitis in the region of the internal acoustic meatus.

HUNTER, Philadelphia.

PNEUMOCOCCIC MENINGITIS WITH RECOVERY: COMBINED USE OF SERUM AND SULFANILAMIDE. SIDNEY KREININ, Arch. Otolaryng. **29**:371 (Feb.) 1939.

Kreinin reports a case of pneumococcic meningitis which was cured by sulfanilamide. The spinal fluid contained 15,000 cells. A total of 160,000 units of type V and type VII pneumococcus serum was used intramuscularly and intraspinally, together with sulfanilamide. Prontosil soluble (the disodium salt of 4-

sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonic acid), 15 cc. of a 2.5 per cent solution, was given every four hours. The patient had bilateral purulent frontal sinusitis and right maxillary sinusitis. A type VII pneumococcus was recovered from the spinal fluid. Sulfanilamide was used intraspinally. Although the administration of sulfanilamide and prontosil led to a sterile culture of the spinal fluid, the patient did not respond clinically until serum was used, leading the author to think that the pneumococcic organism is destroyed with sulfanilamide and its toxins neutralized with the serum.

HUNTER, Philadelphia.

VIRUS OF MENINGITIS AND PNEUMONITIS. T. FRANCIS JR. and T. P. MAGILL, J. Exper. Med. **68**:147, 1938.

An infectious agent is described which belongs apparently to the class of filtrable viruses but which, on the basis of the evidence at hand, is not to be identified with any virus previously described. It has multiple tropisms and is pathogenic for mice, for ferrets and for monkeys of the species Macacus rhesus and Macacus cynomolgos. Mice and ferrets infected intranasally show extensive pneumonic lesions of fatal severity. Monkeys inoculated intracerebrally show lymphocytic choriomeningitis, from which they recover, while mice similarly inoculated show rapidly fatal choriomeningitis. Mice which receive the virus by intraperitoneal or subcutaneous routes show fatal paralysis in a moderate proportion of their number, while the remainder become immune according to the intracerebral test but not according to the intranasal test. In mice, monkeys, ferrets, rabbits and guinea pigs subcutaneous inoculation causes local granulomatous induration of the skin with enlargement of the regional lymph nodes. In 1936 ferrets inoculated with throat washings of patients suffering from an epidemic disease clinically indistinguishable from epidemic influenza yielded the virus repeatedly. It is impossible, however, to draw any conclusion as to whether the virus has its origin in ferrets or in man. Although the new agent possesses many features in common with the virus of lymphocytic choriomeningitis and the virus of lymphogranuloma venereum, cross immunity tests have failed to yield any evidence that it is immunologically related to either of these viruses. For purposes of identification, the name "virus of acute meningopneumonitis" is suggested.

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

MUMPS MENINGO-ENCEPHALITIS. T. L. BIRNBERG, Minnesota Med. **22**:173 (March) 1939.

During a period of five and a half years, Birnberg has encountered 38 cases of mumps meningoencephalitis in private practice. So large an incidence, with no coincident unusual epidemic of mumps, leads him to consider mumps as a disease in which meningeal symptoms appear relatively often. In the preadolescent age group it has been the most frequent complication that he has observed. The specific cause of mumps meningoencephalitis seems to be either the mumps virus or a toxin liberated by the virus. The clinical symptoms of mumps meningoencephalitis may appear at from one to ten days after the onset of the parotitis. Occasionally the meningitis and the parotitis develop simultaneously, as in 1 of the present cases. The neurologic symptoms in rare instances precede the parotitis by several days. There are some cases in which the meningoencephalitis appears to be of undoubted mumps origin by virtue of epidemiologic contact but in which parotitis never occurs or is so slight as to pass unnoticed. The symptomatology, as observed in the 38 cases, shows a fair degree of uniformity. The presenting symptom is almost invariably headache, often intense. Vomiting occurred in practically all cases, but was usually not incessant and persisted for only one or two days. All patients had varying degrees of fever. Hiccup, lethargy and irritability were inconstant and usually not pronounced symptoms. Rarely dilated pupils may be an index of cerebral involvement. Convulsions and focal paralysis have been recorded, but the author did not observe them in his cases. Neurologic

examination almost always reveals rigidity of the neck and a positive Kernig sign. The diagnosis rests largely on the recognition that such a complication occurs. The relative mildness of the symptoms with a rather high cell count is a valuable diagnostic criterion. The treatment of mumps meningoencephalitis is chiefly symptomatic. Spinal puncture should be performed as a diagnostic procedure; it is often of value in reducing fluid pressure, particularly in patients with persistent headache and vomiting. Mumps meningoencephalitis persists for from three to eleven days. The temperature returns to normal, and the subjective symptoms disappear two or three days before the neurologic signs become normal.

J. A. M. A.

MENINGOENCEPHALITIC COMPLICATIONS OF TYPHOID IN CHILDREN. E. PELUFFO and C. E. CASTELLS, Arch. de pediat. d. Uruguay **10**:35 (Jan.) 1939.

According to Peluffo and Castells, typhoid bacteria have a special affinity for the nervous system, especially in children. The most frequent complications of typhoid in children are those involving the meninges or the brain, with development of a special type of encephalitis. The acuteness of the complications varies in different cases. Meningitis is more frequent and less grave than the encephalitic complications. It may develop at any time in the course of typhoid. Sometimes the meningeal reactions are the predominant symptoms of typhoid, and again grave suppurative meningitis may develop. The encephalitic complications may cause bulbar, cerebellar ataxic, mesencephalic, choreic, cortical aphasic, mental and epileptic symptoms. The prognosis of the complications, especially encephalitis, is grave. Until recently symptomatic treatment was resorted to, but satisfactory results have now been reported in the literature in cases of typhoid encephalitis from immunotransfusion. The authors report 4 cases of the disease in children between the ages of 3 and 4 years. In none of the patients was immunotransfusion resorted to. Three patients died. The one who recovered had mental sequelae.

J. A. M. A.

COMPARATIVE INVESTIGATIONS ON PRIMARY SEROUS MENINGITIS AND PARALYTIC POLIOMYELITIS. H. C. A. LASSEN, Ugesk. f. læger **101**:73 (Jan. 19) 1939.

Lassen finds that endemic clinical paralytic poliomyelitis agrees with endemic primary serous meningitis in apportionment as to age, sex and the different social classes, and in most of the symptoms and objective signs before and during hospitalization. While no certain differences between the two groups of cases appear, endemic poliomyelitis is more seasonal than primary serous meningitis, and the average cell count of the spinal fluid is higher at the clinical start of the disease, with even decrease from this time. In primary serous meningitis the cell count does not reach its maximum until from the seventh to the ninth day. There is a greater tendency in the paralytic form to increased values for albumin, globulin and sugar in the spinal fluid. In the majority of cases primary serous meningitis in Denmark is at present regarded as probably of poliomyelitic origin.

J. A. M. A.

Diseases of the Brain

OUTBREAK OF ENCEPHALITIS IN MAN DUE TO THE EASTERN VIRUS OF EQUINE ENCEPHALOMYELITIS. R. F. FEEMSTER, Am. J. Pub. Health **28**:1403 (Dec.) 1938.

Feemster gives a chronologic review of the 1938 outbreak in Massachusetts of encephalitis in horse and man due to the eastern virus of equine encephalomyelitis. He states that it is impossible at present to estimate how many human cases of encephalitis due to the equine virus have occurred in the state during the outbreak. About 38 cases have been under investigation. Thus far the

virus has been isolated at postmortem examination in eight cases. If the mosquito is the vector of the natural infection in horses, the spread of the disease in the state can easily be accounted for once a case is introduced. Some of the cases under investigation will have to be eliminated either because another diagnosis will be established or because evidence will not be sufficient to warrant the diagnosis of encephalitis due to the equine virus. As early as 1931 Meyer suggested the possibility of human beings contracting the equine disease. The disease in the severer form is sufficiently different from the usual varieties of encephalitis to be recognized clinically. If some of the milder forms in the cases under investigation prove to be due to the same virus, particularly if the existence of subclinical infections can be established, the recognition of all cases will be difficult unless laboratory means of verifying the diagnosis can be found. The onset in infants was sudden, and was accompanied by fever, irritability or drowsiness, cyanosis and convulsions. In older children and in the 1 adult the symptoms were of slower onset, from four to ten days. Headache, frontal in character, and dizziness were the first complaints in the older patients. All patients were semicomatose or comatose on admission, and the majority showed continued tremors or muscular twitchings. Rigidity of the neck was a constant feature, as was a tense anterior fontanel in the infants. Suppression of the cutaneous reflexes was constant in the comatose patients, while the Kernig and kindred signs varied greatly. The pupils reacted sluggishly to light. The temperature was invariably high, from 102 to 104 F., and in the cases of fatal outcome (25 of the 38) it continued to rise. When recovery took place the fever fell by lysis, becoming normal in four or five days. The spinal fluid showed increased pressure. When the patient lived for more than two or three days there was a drop in both the spinal fluid cells and the leukocytes, with a change to the mononuclear type. Convulsions and muscular twitchings marked the course of the disease. In the infants a peculiar edema developed about the eyes and in the upper extremities. Cyanosis was marked in all cases. Deep coma, from which the majority of patients did not arouse, developed shortly after admission. In some cases in which the diseases was suspected of being due to the virus there was complete recovery, but it appears that in others there will be paralyses, mental changes and other permanent residuals. A number of problems with regard to the disease await elucidation. It is necessary to know whether reservoirs other than the horse are important. It remains to be demonstrated satisfactorily that the mosquito transmits the natural infection among horses. The importance of other insects, especially the recently incriminated tick, as vectors of the disease awaits investigation. The need of having all cases of encephalitis reported to health departments is emphasized by the presence of the equine infections in human beings. The rate of attack among horses was low (3.5 per cent), but the fatality rate was high (more than 90 per cent).

J. A. M. A.

HEMORRHAGIC ENCEPHALITIS IN PREGNANCY FOLLOWING ANTISYPHILITIC THERAPY WITH NEOARSPHENAMINE. SAMUEL S. PALEY and NORMAN PLESHETTE, Am. J. Syph., Gonor. & Ven. Dis. **23**:69 (Jan.) 1939.

Paley and Pleshette found reports of 158 cases of hemorrhagic encephalitis resulting from arsphenamine therapy since 1911. They noted that in a large proportion of cases the disease in women was associated with the treatment of syphilis during pregnancy, and they described a similar case of their own. Of the women affected, over 70 per cent were pregnant. The pregnant women were usually young primiparas who had not received any previous antisyphilitic therapy and who presented no clinical evidence of syphilis except a positive Wassermann reaction. Preliminary treatment with a bismuth preparation had no effect in preventing the development of hemorrhagic encephalitis. The dose of neoarsphenamine was 0.45 Gm., or more. Most of the patients received only two or three injections, and symptoms usually developed about forty-eight hours after the last injection. Prodromal symptoms were headache, malaise, fever,

dizziness and generalized body pains, followed by restlessness, coma and convulsions. In practically all cases the termination was fatal. The most frequent sites of involvement in the central nervous system were the corpus callosum, the caudate and lenticular nuclei, the pons and the medulla. These areas showed diapedesis of red cells about dilated capillaries.

The authors caution against large doses of neoarsphenamine in young pregnant women. They suggest that, as the pathologic lesion of hemorrhagic encephalitis is capillary hemorrhage, it is possible that drugs like snake venom and calcium preparations may prove of value.

BECK, Buffalo.

CEREBROVASCULAR COMPLICATIONS IN THROMBO-ANGIITIS OBLITERANS. E. HAUSNER and E. V. ALLEN, Ann. Int. Med. **12**:845 (Dec.) 1938.

Hausner and Allen conclude, from a study of the 23 cases of involvement of the cerebral arteries with thromboangiitis obliterans of the extremities reported in the literature, that lesions of the cerebral vessels, while not always characteristic of thromboangiitis obliterans, may affect persons with this disease of the extremities who do not have syphilis, hypertension, diabetes or other detectable causes for cerebrovascular lesions. They have observed 11 cases of thromboangiitis obliterans involving the extremities in which there was evidence of vascular lesions involving the brain. The duration of the peripheral disease in their cases varied from five months to twenty years. The ages of the patients varied from 35 to 59 years. In most of the cases the cerebral complications occurred after the onset of the peripheral disease. The cerebral lesion preceded the peripheral symptoms in only 3 cases. In these 3 cases the hemiplegia was present two, one and fourteen years, respectively, before the onset of the peripheral symptoms. Thromboangiitis obliterans must therefore be suspected in cases of cerebrovascular disease of obscure origin. The main neurologic symptom was hemiplegia, which occurred transiently, once or several times, or permanently. In some cases there were confusion, disorientation, aphasia and loss of memory, symptoms which frequently cleared up entirely. Hemianopia, present in 2 cases, disappeared in 1 case after sympathectomy. The symptoms of thromboangiitis in the brain depend chiefly on the location of the lesion in the brain. The 11 patients with cerebral involvement were from a group of 500 persons with thromboangiitis obliterans of the extremities. It may be found that this complication occurs more frequently if attention is directed to it. The study emphasizes that cerebrovascular complications may occur in cases of thromboangiitis obliterans and may precede evidence of the disease in the extremities. It is also apparent that peripheral thromboangiitis obliterans may be the least serious part of a disease which may be disabling or may terminate life as a result of cerebral or cardiac involvement.

J. A. M. A.

SUPPURATION OF THE PETROUS PYRAMID. ROBERT L. MOORHEAD and JOHN P. BAKER, Arch. Otolaryng. **28**:497 (Oct.) 1938.

Experience has shown that the conclusions of earlier operators on patients with petrositis have not always been corroborated. In 30 consecutive cases operation for petrositis was performed, and pus was seen in the pyramid. In all but 3 cases a mastoid operation had been performed. In 4 cases reinfection of the petrosa occurred after the mastoid had healed. The authors do not regard pain in the eye as diagnostic, because in their series the pain was in the frontal region and around the eye. It was found even in the opposite eye. Pain in the teeth was noticed in 4 cases. Diminution of discharge from the middle ear was not a bad sign unless it was accompanied by an increase in other symptoms. Palsy of the external rectus muscle was found frequently in this series (in 14 cases). The roentgenogram was found to be an unsatisfactory aid. The time of onset of the various symptoms was of as much significance as the signs themselves; pain immediately after a mastoidectomy was less important than pain three or four weeks after operation.

The authors advocate a simple mastoid operation unless meningeal signs are present. It is better to explore the petrosa than to wait for meningitis to develop. No untoward effects from the wide exposure of the dura have been noted. The cisterna pontis is drained. Radical mastoidectomy is rarely indicated. The few cases in which the peritubal area is involved do not warrant the rule for radical mastoidectomy on every patient.

HUNTER, Philadelphia.

ABSCESS OF THE BRAIN: RELATION OF THE HISTOLOGIC TO THE CLINICAL FEATURES. BERNARD J. ALPERS, Arch. Otolaryng. **29**:199 (Feb.) 1939.

Alpers studied 27 cases of histologically verified abscesses of the brain to determine how and when encapsulation occurs and what relation the abscess has to the bacterial content, in order to determine when to advise operation. Abscesses of the brain become encapsulated in the course of time. Capsules have been seen at an early stage in some cases, and not at a similar stage in others. This is because the formation of the capsule is dependent on the following variable factors: 1. The nature of the invading organism. Some organisms are more prone to induce capsule formation than others. 2. The resistance of the host. This is probably an important factor in the capsule formation, but it is an intangible element, which is not easily measured and hence is difficult to evaluate. The more resistance the organism meets, the more likelihood there is of capsule formation. In the series reported by Alpers, an abscess of three days' duration showed no capsule; another showed beginning encapsulation in six days; another, no sign of capsule in ten days, and another, a good capsule in fourteen days. In 3 cases there was good encapsulation in twenty-one days, in 1 case a poorly formed capsule after two months, in another no capsule whatever after two and one-half months, and in another poor encapsulation after eleven months; 11 other abscesses of from two to eleven months' duration showed good encapsulation, especially in the case of traumatic abscess. No definite rule can be stated in regard to the relation of encapsulation and the duration of the abscess. Time is an important factor; while it is possible to say that the older the abscess the greater the likelihood of encapsulation, other factors, such as the virulence of the organism and the resistance of the host, are important in the development of the abscess.

The type of organism has an important bearing on the formation of the capsule. Alpers finds that the staphylococcus is accompanied by poor capsule formation. Other authors, however, have observed the reverse to be true. Cocci are said to tend to produce encapsulation, and the anaerobic group is said to proceed directly to encephalitis with no capsule formation. A virulent organism in the blood stream will cause death before an adequate capsule can be formed. Abscess of the brain is more frequently a complication of chronic than of acute otitis media or mastoiditis. Abscesses with mixed infections do not form capsules as well as those with a single organism.

The capsule is composed largely of connective tissue. Careful examination with special stains showed no evidence of neuroglia elements in the capsule. In fact, gliosis was not observed even in the surrounding brain tissue, except in a few cases of chronic abscess in which its presence was interpreted as an uncommon factor of encapsulation. Other authors, however, have observed varying proportions of neuroglia fibrils in the capsule. The observations in Alpers' cases do not support this view. The capsule is derived from the blood vessels, lymphocytes and the dura and pia mater. It has been stated that time is the most important element in the formation of the capsule of an abscess. Hence, it seems reasonable to assume that in cases of acute abscess the longer one waits before operation the better the chance of encountering a walled-off abscess. This is true in most cases, but there are well known instances in which no encapsulation or inadequate encapsulation has occurred after several months. In most cases, if the situation is not too acute, it seems advisable to wait at least three weeks, and preferably four, for encapsulation before operating. This is not always

possible, because in some cases the onset is so acute and the situation so desperate that immediate intervention seems necessary.

An encapsulated abscess is not by any means a quiescent abscess. Within the cavity of the abscess may be virulent bacteria, which if permitted to escape into the meninges may produce fatal meningitis. Practically all abscesses contain bacteria. Only occasionally is a sterile abscess encountered. This fact is intimately associated with the problem of encephalitis around some abscesses. Even in the case of old abscesses one sometimes observes active encephalitis in the tissue around the capsule. It seems desirable to know whether such encephalitis is present in certain cases in order to be prepared for it in the operative approach. Thus far, however, no signs have been found which can be regarded as characteristic of this encephalitic reaction.

HUNTER, Philadelphia.

DISTURBANCES OF MICTURITION ASSOCIATED WITH DISSEMINATED SCLEROSIS. ORTHELLO R. LANGWORTHY, J. Nerv. & Ment. Dis. **88**:760 (Dec.) 1938.

In a study of the histories in 157 cases of multiple sclerosis in early or ambulatory stages, Langworthy found that 97 patients, or 62 per cent, mentioned some form of vesical disturbances, although urinary symptoms had not been stressed when the histories were taken. There was urgency in 52 cases, hesitancy in 39, incontinence in 33, frequency in 32, dribbling in 7 and acute retention in 7.

Among diseases of the central nervous system, syphilis produces the largest group of disturbances of micturition, and disseminated sclerosis, the second largest group. Vesical abnormalities are characteristic, however, not of the disease but of the anatomic lesion. The changes in the function of the bladder in disseminated sclerosis, when studied kymographically, fall into three main groups. Bilateral injury of the corticospinal tracts diminishes voluntary control over the bladder and increases the tone of the external sphincter as well as that of the musculature of the wall of the bladder, thus making the stretch reflex of the bladder more irritable. In this condition there are frequency and urgency and small capacity of the bladder, but usually no residual urine unless other pathways in the spinal cord are injured. Emotional and intellectual stimulation increases the irritability of the vesical musculature. The second group includes cases in which bilateral lesions in the lateral columns injure both the corticospinal fibers and efferent tracts from the midbrain which control tone in the muscle of the bladder. In this condition the symptoms found in the first group are seen, and, in addition, the vesical contractions are irregular and poorly sustained and are therefore inefficient in emptying the bladder, leaving a residuum of urine. There are frequency and urgency and often dribbling or incontinence, since the patient is unable to control the contractions of the bladder. In the third group injury to the cerebellum or its connections produces hesitancy or retention. Graphic records show a bladder of large volume and low intravesical pressure and feeble contractions.

In disseminated sclerosis, combinations of these disturbances of function occur, depending on the distribution of the lesions. Graphic studies are valuable in determining the proper treatment in the individual case. Hyperirritability of the bladder may be controlled by atropine, with or without ephedrine. The feeble, atonic bladder may be aided by mecholyl, which stimulates the parasympathetic mechanism.

MACKAY, Chicago.

HYDRATION STUDIES IN EPILEPSY. E. ZISKIND, E. SOMERFELD-ZISKIND and R. BOLTON, J. Nerv. & Ment. Dis. **89**:52 (Jan.) 1939.

The Ziskinds and Bolton draw certain deductions relative to dehydration in treatment of epilepsy from the study of 16 epileptic patients and 9 normal subjects who drank, after an overnight fast, 7,000 cc. of tap water, at a uniform rate of 1,000 cc. each half-hour. Body weight, urinary output and specific gravity were

recorded at intervals of thirty minutes. Convulsions followed hydration in half the epileptic patients. There were no convulsions in the 9 normal subjects. Dilution of the blood and water retention were greater in the epileptic than in the nonepileptic subjects. This observation, if substantiated, may have important bearing on the question of increased cell permeability in persons with epilepsy. Blood dilution and water retention were greater in epileptic patients having seizures subsequent to hydration than in those not so affected. Although excessive amounts of water were a positive factor in precipitating seizures, average amounts did not have this effect. The results cast doubt on the efficacy of dehydration in controlling convulsions.

J. A. M.A.

"APHASIA" IN A PARTIAL DEAF-MUTE. MACDONALD CRITCHLEY, Brain **61**:163, 1938.

Hughlings Jackson suggested that focal cerebral lesions may damage or destroy the execution of sign language by a deaf-mute. Critchley reports a case in which strong support is furnished for Jackson's contention, although complete proof is lacking.

A man aged 42 had been well until the age of 7, when he gradually lost his hearing and was taught finger spelling. At 14 he was stone deaf and was admitted to an institution for deaf-mutes, where he was taught lip reading. After leaving the school he relied chiefly on manual signs and finger speech to communicate with others. Paralysis developed on the right side, and for three days he was deprived of what little articulate speech had previously been possible to him. Paralysis, like speech, improved to a certain degree. As soon as he was able to hold a pen it was found that he could neither write nor perform on paper simple arithmetic calculations. He could no longer read lips. For a few days after the stroke he was unable to understand people who communicated with him by finger spelling. This ability returned in a few days, but he was still unable to reply on his hands. Articulate speech was infrequent and considerably altered. Speech was dysarthric and ungrammatical; he seemed to rely little on this means of communication. He remained under observation for the next two years, during which his condition changed little, if at all.

No similar case is recorded in the literature. Grasset (1896) reported the case of a deaf-mute who lost his ability to make hand signs after a cerebral vascular lesion. The patient was able to read with understanding and to comprehend finger talk in others. He was unable, however, to reply in the finger alphabet with the right hand, but could do so with the left. Grasset concluded that in the deaf-mute a center for manual speech develops in the cortex, independent of the motor area of the upper limb. He located this tentatively at the foot of the second frontal convolution of the left hemisphere.

In Critchley's case, the natural sign language was not impaired. The circumstances were unusual, however, in that the patient had never been proficient in this means of communication and preferred lip reading or finger spelling. This may be ascribed to a variety of reasons, especially to the fact that hearing was intact for the first few years of life, during which articulate speech developed normally. For this reason, the patient cannot be regarded as having "complete" or congenital deaf-mutism. Hughlings Jackson's surmise therefore remains unverified, as it referred explicitly to a natural system of signs and not to finger spelling. It is justifiable to suggest that a much more severe lesion would be required to abolish the primitive sign language than the elaborate system of dactylology.

SALL, Philadelphia.

PERSISTENT MIRROR-MOVEMENTS AS A HEREDOFAMILIAL DISORDER. E. GUTTMANN, W. S. MACLAY and A. B. STOKES, J. Neurol. & Psychiat. **2**:13 (Jan.) 1939.

Guttmann, Maclay and Stokes describe a syndrome of persistent, symmetric associated mirror movements in the case of a man aged 49 who came under obser-

vation because of an attack of endogenous depression. The mirror movements involved only the upper extremities and consisted of an associated symmetric movement of one limb on both active and passive movements of its fellow. Similar results were obtained on electrical stimulation and in writing or drawing. The movements usually occurred in symmetric muscles, but occasionally parallel movements were obtained through innervation of the antagonists. The associated movements of the left hand accompanying active movements of the right were stronger than those in the converse situation.

The patient manifested no organic signs other than the mirror movements, the onset of which was unknown. This played no part in the symptoms of the mental illness, though it may have contributed to the makeup of the prepsychotic personality, which was characterized by indecision of action. The family history revealed a similar disturbance in the father, a paternal uncle, a sister, a brother, a son and a nephew of the patient. This familial trend, evident both from observations recorded in the literature and from study of the present case, points to a single dominant, non-sex-linked factor as responsible for the syndrome.

It is known that mirror movements are physiologic in children up to the age of puberty. However, the infantile mirror movements are characterized by a converse variation of intensity with regard to the dominant hand, and they never occur with passive movements. Therefore the familial type cannot be regarded as an inherited developmental delay.

Guttmann, Maclay and Stokes regard this familial synkinesia as a classic example of associated movements in Kinnier Wilson's sense, namely, as "those involuntary movements of one limb which may be seen to accompany forceful voluntary movements of its fellow on the other side." The authors emphasize the distinction between these movements and those occurring under pathologic conditions. They disagree with Foerster's classification of the synkinesias and propose the following: (*A*) Normal: (1) components of movements; (2) movements of cooperation; (3) transient mirror movements in children and in adults when acquiring new patterns of movements. (*B*) Abnormal: (1) symmetric without spreading (parkinsonian type); (2) symmetric with spreading; (3) persistent mirror movements. The authors believe that the physiology of the passive associated movements differs fundamentally in no way from that of the active, and consider both to be of reflex origin, with the same central connection.

MALAMUD, Ann Arbor, Mich.

WERNICKE'S ENCEPHALOPATHY (POLIO-ENCEPHALITIS HAEMORRHAGICA SUPERIOR): ITS ALCOHOLIC AND NONALCOHOLIC INCIDENCE. A. C. P. CAMPBELL and J. H. BIGGART, J. Path. & Bact. **48**:245 (March) 1939.

Campbell and Biggart cite 12 cases of Wernicke's encephalopathy, in only 1 of which frank chronic alcoholism could be established; in the others alcohol could be completely eliminated as a causal factor. In the latter cases complications of a wide range of primary conditions were present: gastric carcinoma (3 cases); chronic dyspepsia with gallstones and an old gastroenterostomy; pernicious anemia; macrocytic anemia following resection of the bowel; pregnancy (2 cases; hyperemesis was present in 1 case); bronchiectasis; chronic pyosalpinx, and a vague illness, possibly whooping cough, in a child. The pathogenesis of the encephalopathy is not clear. However, of the pathogenic factors which may be present singly or in combination, vitamin deficiency, especially of vitamin B_1, seems to be the most obvious possible common factor in the range of primary diseases which lead to the encephalopathy. Wernicke's encephalopathy is a clearcut pathologic entity which, unless specifically looked for, may easily be missed at postmortem examination.

J. A. M. A.

PEARLY TUMORS OF THE CENTRAL NERVOUS SYSTEM. HARDEN ASKENASY, Encéphale **1**:209, 1938.

Of 2,500 operations on the central nervous system, 6 revealed the presence of pearly tumors—5 in the cranial cavity and 1 in the spinal canal. All 6 tumors were epidermoid cysts. None contained hair or other epidermal adnexa. The patients' ages varied from 11 to 39 years. In 1 case a tumor deep in the left frontal lobe was associated with a mental syndrome consisting of amnesia, disorientation in space, character disturbances and anosognosia, in addition to headache, declining vision and right central facial paralysis. The wall of the cyst was removed and the contents curetted. The mental disturbances regressed quickly. The patient was alive seven years later, but was practically blind. The second patient had an enormous tumor over the quadrigeminal plate. It invaded the caudal portion of the third ventricle and both thalami and obstructed the sylvian aqueduct and the fourth ventricle. The patient, a woman aged 39, had suffered from generalized epilepsy since childhood. Her father and 4 siblings were likewise affected. Two months before operation headache suddenly appeared, and vision diminished in the left eye. There was juxtapapillary choroiditis and the Wassermann reaction of the blood was positive, but antisyphilitic treatment did not result in improvement. The tumor was localized by a ventriculogram. The patient died in status epilepticus after partial ablation of the tumor. The veins of Galen and their affluent tributaries were turgescent. There was an enormous cereballar cone of pressure. In another case, that of a boy aged 11, there was a five months' history of intermittent amblyopia and blindness, beginning and ending suddenly, headache, lacrimation, vomiting, abdominal pains and somnolence. Examination revealed bitemporal hemianopia and atrophy of the optic nerves. The tumor was suprasellar, overlying the chiasm and the left optic nerve and adhering to the tuberculum sellae and the jugum sphenoidale. The cyst was partially removed, leaving the portions which were in contact with the optic nerves, the base of the third ventricle and the large vessels. The patient was well, but vision was unimproved (1/50) one month later. In this instance most of the criteria were presented for the clinical diagnosis of suprasellar cholesteatoma set forth by Olivecrona, but the case was peculiar in that, except for slight disjunction of the sutures, the roentgenogram of the skull was normal. Two other patients had tumors of the cerebellopontile angle. They presented headache, papilledema, vomiting, tinnitus, vertigo, cerebellar disturbances and, in 1 case, somnolence and polydipsia. One of these patients died of respiratory failure at the end of the operation. The fate of the other patient is not stated. The epidermoid in the spinal cord was observed in a 37 year old patient who had spastic paraplegia with sphincter, genital and sensory disturbances and was found to have an intramedullary tumor at the level of the sixth and seventh thoracic laminas on the right side. The cord was incised and the mass removed with the curet. One month later most of the symptoms had regressed. An important feature of pearly tumors is their long, silent growth, followed by the rapid development of symptoms at a stage when they are large and often adhere to vital structures. While surgical treatment is the only efficacious method, total removal of the tumor is usually not feasible, at least in a single operation.

LIBER, New York.

Disease of the Spinal Cord

FLUID BALANCE IN MÉNIÈRE'S DISEASE. T. CAWTHORNE and MARY N. FAWCETT, Lancet **2**:1404 (Dec. 17) 1938.

Cawthorne and Fawcett studied the effect of various salt and fluid intakes on the symptoms of Ménière's disease in 11 patients. All but 1 were affected to a greater or less degree by variations in the intake of fluid and sodium chloride. Any steps taken to favor the retention of fluid within the body resulted in aggravation of the symptoms, whereas the reverse was true when excretion of fluid was encouraged. In 9 cases this fluctuation of the symptoms was accom-

panied by variation in the hearing capacity; thus, when the symptoms were more marked the hearing was worse, and vice versa. None of the patients under review tended to retain fluid unduly, although they were all sensitive to variations in the salt and fluid intake. It seems that imperfect functioning of the pressure-regulating mechanism of the endolymphatic system places the affected labyrinth under the influence of any factors that may effect the secretion or absorption of endolymph on that side. It is not unreasonable to suppose that an increase of the fluid content of the body may favor an increase of the intralabyrinthine pressure. It is recommended that an antiretentional regimen should form part of the investigation of every patient with Ménière's disease. J. A. M. A.

INJURIES OF THE CERVICAL PORTION OF THE SPINAL CORD IN NEWBORN CHILDREN. F. HAUSBRANDT, Deutsche Ztschr. f. d. ges. gerichtl. Med. **29**:353, 1938.

Hausbrandt believes that at times minor alterations in the cervical portion of the spinal cord in newborn children are regarded by pathologists as a cause of death, although, practically, they have no significance. Not every tear of the tentorium leads to death, as such tears have been encountered in children who survived up to twenty days and then died of intercurrent infections. This is especially true of premature infants. When, on the other hand, the physiologic tension of the tentorium is altered because of tears in it, pressure on the head in the birth canal is applied to the medulla oblongata so that the stimulus to respiration is initiated. The same pressure effects may be at work when there is massive hemorrhage in the posterior cranial fossa. The term "aspiration of amniotic fluid" does not indicate either a definite process or a clearcut diagnosis.

After a detailed technical consideration of the method to be employed in removing the spinal cord, the author discusses the pathologic changes he has encountered. Hemorrhage was observed in the epidural space of the cervical region in some of the bodies examined, but it was not a regular accompaniment of intracranial hemorrhage. Usually such hemorrhages were associated with extensive injuries of the cervical part of the spinal cord; they occupied the upper portion and showed gradation from bloody edema to massive, sleevelike hemorrhages. Subdural hemorrhages were less frequent and extensive than epidural ones and usually were continuations of infratentorial extravasations. Hemorrhages in the meninges were relatively rare. Injury of the cord near its junction with the medulla was seen frequently in full term stillborn children and in those dying shortly after birth. Regions of softening and hemorrhage were found most often at the junction of gray and white matter. The white substance was usually spared, but isolated or clumped hemorrhages were common in the region of the posterior horn.

RUKSTINAT, Chicago. [ARCH. PATH.]

POLIOMYELITIS IN DENMARK IN 1937, WITH SPECIAL REGARD TO EPIDEMIOLOGIC RELATION AND LOCALIZATION OF PARESES. H. C. A. LASSEN, Ugesk. f. læger **101**:80 (Jan. 19) 1939.

Lassen states that the highest incidence of poliomyelitis to date in Copenhagen was in 1937. The disease was not endemic in the schools. One hundred and twenty-six paralytic patients and 60 patients with primary serous meningitis, believed to be of poliomyelitic origin, were treated at Blegdam Hospital. In at least 80 per cent of the patients with pareses the first signs of certain paresis occurred within the first six days of the disease. If after the first indications of paresis there is an interval of two or three days without progression, extension of the paresis is unlikely. About half of the paretic patients showed symptoms of disorder of the bulbopontile portion of the central nervous system; 44 per cent had paralysis of a cerebral nerve; in two thirds of these there was disorder of the facial nerve, and in one-sixth of the abducens nerve, and about one fourth of the patients had respiratory difficulty. Nineteen of these were treated in the respirator, and 2 with artificial manual respiration. In two fifths of the cases there was complete restitution on discharge or complete restitution later was probable; in one fifth

restitution was doubtful, and in one fifth it was considered improbable. Examination, a year later, in the main confirmed this prognosis. One fifth of the paretic patients died, the highest mortality being in the age group over 20. In 18 cases death was due to respiratory paresis with complications; in 7 to hyperpyrexia or bulbar paresis with respiratory difficulty. In 21 cases death occurred before the tenth day. In all these cases bulbar symptoms were more or less prominent. Of the 19 patients given respirator treatment 6 survived. The real field for the respirator, the author says, is for patients with spinal respiratory paralysis without bulbar symptoms. Most of the patients who died in the respirator showed increasing cyanosis without definite signs of circulatory insufficiency, and in spite of apparently sufficient ventilation. It is suggested that in cases in which swallowing or coughing is impossible the respirator by its inspiration suction aspirates secretion from the upper respiratory passages into the smaller bronchi, thus compromising the arterial oxygen saturation.

J. A. M. A.

Peripheral and Cranial Nerves

CAUSE OF PARALYSIS IN DIPHTHERIA. I. TAYLOR, Brit. J. Child. Dis. **35**:250 (Oct.-Dec.) 1938.

Taylor discusses some of the evidence bearing on the manner in which diphtheria toxin attacks the nervous system. The view held by some authors is that all forms of diphtheritic paralysis are due to hematogenous toxemia, the frequency with which certain nerves are attacked being explained by the selective affinity of the toxin for these nerves. The close anatomic relationship between the site of infection and the initial paralysis has led other observers to discard this theory in favor of views of a different nature. They state that the toxin first attacks the nerves in the locality of the site of infection and that all other paralyses are produced by diffusion of toxin in the nervous system from the point of entry. This view receives some support from the orderly sequence of paralyses commonly noted in faucial diphtheria. The two schools of thought meet in the theories advanced by Walshe that (1) the initial paralysis is caused by lymphogenous invasion of the nervous system, the toxin passing from the site of infection to the central nervous system by the perineural lymphatics; (2) generalized paralysis is the result of hematogenous toxemia, and (3) accommodation paralysis is the result of the selective affinity of circulating toxin for certain elements of the nervous system. Most clinicians and experimental workers are agreed that the late multiple neuritis following diphtheria, giving rise to diphtheritic pseudotabes, is due to hematogenous toxemia. The strongest evidence of the hematogenous origin of such paralyses is the fact that the experimental injection of diphtheria toxin intravenously in animals produces a multiple neuritis which is exactly comparable with this late form of peripheral neuritis accompanying diphtheria in the human being. In addition to paralysis of the limbs, accommodation paralysis must be included in the group of symptoms due to blood-borne toxin, because this form of paralysis is found frequently in both faucial and extrafaucial diphtheria. There are good grounds for believing that hematogenous toxemia is capable of producing, in addition to generalized paralysis, a type similar to the local paralysis found in faucial diphtheria. The author believes that one may thus accept the possibility that blood-borne toxin may play a part in the production of local paralyses as they are encountered in faucial diphtheria. The close anatomic relation between the local paralysis and the site of infection can leave no doubt that the nervous system is primarily attacked by local absorption of toxin. Unilateral faucial diphtheria frequently results in paralysis of the corresponding side of the palate. An important and familiar clinical observation is what has been described as the "march of paralysis." One cannot but be impressed by the orderly way in which paralysis develops in most severe forms of the disease, palatal paralysis preceding pharyngeal and the diaphragm being involved before the intercostal spaces. Such a march suggests the slow spread of toxin in the central nervous system.

J. A. M. A.

VITAMIN C NUTRITION AND SUSCEPTIBILITY TO DIPHTHERIA AS POSSIBLE FACTORS IN EPIDEMIOLOGY OF POLIOMYELITIS. W. G. HEASLIP, Australian J. Exper. Biol. & M. Sc. **16**:287 (Dec.) 1938.

Heaslip states that toward the end of 1937 an epidemic of poliomyelitis began in South Australia. A number of the earlier cases occurred in an area of a city in which immunization against diphtheria had been carried out previous to the epidemic, and Dwyer observed that the majority of the cases of poliomyelitis were those of children who were not immunized to diphtheria. Immunization had been carried out without previous Schick tests. In 1937 Jungeblut reported that vitamin C had a therapeutic effect when injected subcutaneously into monkeys inoculated with the virus of poliomyelitis. A review of the literature on susceptibility to diphtheria and to poliomyelitis showed in each case a correlation with the results of certain experimental work with vitamin C. In 1917 Zingher reported that a positive reaction to the Schick test was given in a disproportionately large percentage of cases of poliomyelitis. Comparing the patients with poliomyelitis who were not immunized to diphtheria with the controls, Heaslip finds that the age group of 12 years and over gave substantially the same percentage of positive Schick reactions as the control group. This is possibly the most extraordinary result obtained, as this age group contained 42 per cent of the patients and their ages ranged up to 60 years; 30 per cent of them were 21 years of age or more. Admitting that some of these were rural dwellers, the figure is still high in a state in which diphtheria is moderately prevalent. The same may be said of the whole group, especially when it is considered that fewer than a third of the patients were less than 6 years of age. Of the 238 patients tested, 21 had been artificially immunized, and 9 had had diphtheria. Eight of these 30 gave a positive reaction to the Schick test. In a control group of 359 persons, of whom 4 had had diphtheria and 355 had been artificially immunized, only 2 gave a positive Schick reaction. One of these had received only 0.5 cc. of anatoxin and the other only 1 cc. The author is tempted to suggest that the result in these 2 cases is due to the fact that those who still gave a positive Schick reaction after immunization contracted poliomyelitis. These figures support the idea of a constitutional defect underlying susceptibility to the two diseases, and it is not surprising to learn that several of the patients with poliomyelitis have, within a few months, contracted diphtheria despite immunization. Dwyer reported that few of these immunized patients contracted poliomyelitis. This contrasts sharply with the report of Henry and Johnson that 51 per cent of their patients with poliomyelitis had previously been immunized. The explanation is probably that Dwyer's group was immunized without previous Schick testing; that is, many of them did not require it, whereas it is justifiable to assume that all of the latter group gave positive Schick reactions prior to immunization. From these results, supported as they are by Zingher's observations on a much larger group, it is evident to Heaslip that there is a greater susceptibility to poliomyelitis in persons giving a positive Schick reaction than in those who give a negative reaction. Conversely, there is a larger percentage susceptible to diphtheria among those who contract poliomyelitis than in the normal population. The urinary excretion of vitamin C for various groups of infected and noninfected persons was estimated, and the conclusion is drawn that, while the usual sequence of events is a decreased excretion of vitamin C after infection, it is probable that a low level of vitamin C nutrition predisposes to infection and severity of attack. It is probable that there is a relation between nutrition and the age incidence in this disease.

J. A. M. A.

Vegetative and Endocrine Systems

THE EFFECT OF THE ANTERIOR PITUITARY-LIKE HORMONE ON SPERMATOGENESIS IN THE HUMAN. H. S. RUBINSTEIN, Endocrinology **23**:75 (July) 1938.

Rubinstein reports the effect on spermatogenesis in 6 healthy men of injections of a substance containing the anterior pituitary-like gonadotropic hormone from

the urine of pregnant women. Sperm counts before stimulation were found to increase gradually through a period of six or seven days following an ejaculation. Control counts were listed for one and for six or seven day specimens. One thousand rat units of the preparation in the form of a glycerin solution of the water-soluble fraction of the urine of pregnant women was given intramuscularly each week for from five to nine weeks. The morphologic character, viability and motility of the spermatozoa showed no change, but the total count was increased above normal after periods of treatment varying from four to seven weeks. After injections were stopped the counts remained high in all cases for periods ranging from two to five weeks, after which they returned to the average preinjection level. The author believes that the gonadotropic hormone from the urine of pregnant women, in addition to its interstitial tissue–stimulating effect, also stimulates the tubular epithelium to increased sperm proliferation. It does not hasten the maturity of the particular germinal cells; it stimulates the proliferation of cells at the stage of maturation found in the testis at any particular time.

PALMER, Philadelphia.

CLINICAL, HORMONAL AND HISTOLOGICAL CONDITIONS IN A CASE OF HERMAPHRODITISM. J. CHARVÁT, E. KODÍČEK and O. SCHUBERT, Endocrinology **23**:91 (July) 1938.

Charvát and his associates report a case of pseudohermaphroditism in a woman aged 22. The onset of symptoms occurred at 15 years of age. The most prominent were a masculine body contour, immature mammae, hirsutism, enlarged thyroid, coarse voice and complete amenorrhea. Vascular hypertension, lowered carbohydrate metabolism and increased basal metabolism were also present. Gynecologic studies revealed a penislike clitoris and a small pseudovagina, 3 cm. deep. The patient was treated by irradiation of the hypophysis and adrenals, without effect. She died after surgical removal of the right adrenal gland.

The case was studied clinically, histologically and by serial titration of "sexual hormones" in the urine during a period of one month. The amount of gonadotropic hormone was small (less than 10 rat units), while estrogenic hormone was secreted in an increased quantity (50 to 120 mouse units). The ovary was small, with numerous immature follicles and without the slightest trace of luteinization; the uterus was small and hypoplastic, with an atrophic mucous membrane. The adrenal glands were slightly enlarged and contained cortical adenomas. The hypophysis was enlarged, and the basophilic cells were increased in number. The histologic observation in the ovary was in accordance with the results of titration of the "sexual hormones." In spite of the increased proportion of estrogenic hormone, the uterus was in a state of complete inactivity. The authors believe that the condition of the ovary was due either to lack of gonadotropic hormone or to impaired function of the adrenal cortex. For reasons unknown, the uterus either did not respond by growth to estrogenic hormone or was lacking in some other factor which may be necessary for normal development of the uterus. A considerable amount of androgen was found in the urine, as has been true in other cases of hirsutism.

PALMER, Philadelphia.

STUDIES OF THE EFFECTS OF PITUITARY EXTRACTS ON CARBOHYDRATE AND FAT METABOLISM. A. H. NEUFELD and J. B. COLLIP, Endocrinology **23**:735 (Dec.) 1938.

Neufeld and Collip suggest that the ketogenic effect and the apparent antagonism to epinephrine hyperglycemia and insulin hypoglycemia, as seen in rabbits, are due to one pituitary principle. There is suggestive evidence that the action of the "specific metabolic stimulant," the chromatophore-expanding action, as seen in the frog, and the glycostatic effect of pituitary extracts may all be due to the same principle. These various properties seem to run parallel with the melanophore content of extracts. The active substance is probably the pars intermedia of the hypophysis. Male rats, guinea pigs and rabbits were studied with regard

to the ketogenic properties of preparations of the pituitary. Several extracts of the pituitary were used. The extract labeled 622, the method of preparation of which is described in the report, was especially stable. It was prepared by heating on a boiling water bath, for one hour, the primary aqueous extract (p_H 5) of dissected anterior lobes of the pituitary of the hog, which had previously been dehydrated and defatted with acetone and extracted with alkaline alcohol (p_H 9, universal indicator). A protein precipitate was filtered off, and the filtrate was concentrated until 1 cc. represented 2 Gm. of original tissue; 25 per cent ammonium hydroxide was added to make a 2 per cent concentration of ammonium hydroxide in the solution. After the solution had stood for one hour at room temperature, the precipitate which had formed was removed, and the solution was heated for one hour on a boiling water bath. The ammonia was then removed by vacuum distillation, and the final extract was put into ampules; 0.1 per cent tricresol was added as a preservative. The ampules were heated in an Arnold sterilizer for twenty minutes before capping.

The results indicate that there is obtainable from pituitary tissue a fraction which is thermostable within a wide range of the p_H. This fraction has been demonstrated to have the following physiologic properties: (*a*) production of ketonemia in both normal and adrenalectomized rats; (*b*) production of increased glycosuria and ketonuria in the Houssay dog; (*c*) an antagonistic action on the hypoglycemic action of insulin and on the hyperglycemic action of epinephrine, and (*d*) a glycostatic action which has been demonstrated in rats, guinea pigs and rabbits.

PALMER, Philadelphia.

THE SPECIFIC METABOLIC PRINCIPLE OF THE PITUITARY. L. W. BILLINGSLEY, D. K. O'DONOVAN and J. B. COLLIP, Endocrinology **24**:63 (Jan.) 1939.

The authors report on a study of the active metabolic stimulant isolated from the pituitary gland, termed "the specific metabolic principle." Its specific effect in rabbits is an immediate increase in oxygen consumption and a decrease in the respiratory quotient. Other effects are: (*a*) the production of ketonemia in fasting rats; (*b*) the production of increased glycosuria and ketonuria in Houssay dogs; (*c*) an antagonistic action on the hypoglycemia due to insulin and the hyperglycemia due to epinephrine, and (*d*) a glycostatic action. The study was undertaken on rats and guinea pigs to determine whether other endocrine glands are involved in the metabolic stimulation. The extracts used were made from the dissected anterior lobe of the pituitary gland of the ox.

Thyrotropic extracts were injected in doses of 0.1 cc. daily. On the fourth day the preinjection level of metabolism was 28 per cent above normal. A considerable proportion of the specific metabolic factor could be separated from the thyrotropic hormone. The extract obtained was found to be free from cumulative metabolic stimulation. Normal hypophysectomized and thyroidectomized rats and guinea pigs were studied, and the maximum increase in oxygen consumption was found to occur at about the third hour. The authors ruled out the possibility of any effect of epinephrine on the rising oxygen consumption.

Exposure of the extracts to a temperature of boiling water for one hour at p_H 8 destroyed the thyrotropic activity, but produced no appreciable destruction of the metabolic principle. The authors suggest the standardization of the specific metabolic principle in rabbit units, 1 unit representing the minimal dose given subcutaneously which will cause a maximum metabolic stimulation in three hours in a rabbit weighing 2 Kg. Since the specific metabolic principle does not act through the adrenal medulla, thyroid or pituitary gland and since the hormone of the adrenal cortex is necessary only in amounts sufficient to keep the organism in good condition, it is probable that the effect is exerted directly on the peripheral tissues.

PALMER, Philadelphia.

PSEUDO-SEXUAL PRECOCITY. W. H. REILLY, H. LISSER and F. HINMAN, Endocrinology **24**:91 (Jan.) 1939.

When adrenal cortical tumors develop in young girls pseudosexual precocity occurs, the outstanding characteristics of which are the early appearance of pubic hair and hypertrophy of the clitoris. No other lesion in the young girl can simulate this condition. The term "pseudosexual precocity" is applied specifically to the syndrome associated with adrenal cortical tumors in young girls.

The case reported was characterized by the development at the age of 18 months of a rapidly enlarging clitoris, the development of pubic hair, rapid progress in speech and increase in strength and skeletal growth. The blood pressure varied between 102 systolic and 40 diastolic and 115 systolic and 65 diastolic. The bone age was that of a child of about 4 years. Pyelograms showed a mass, about 6 inches (15 cm.) in diameter, lying above the left kidney. Operation was performed, and a carcinoma of the adrenal cortex, 12 cm. in diameter, was removed. Three months later the patient was given roentgen treatment to the abdomen and lungs. The pubic hair began to disappear; the clitoris became reduced in size, and there was a definitely less masculine manner. At 3½ years of age, twenty-six months after operation, the patient was found to be approximately normal. The blood pressure was 80 systolic and 55 diastolic; there was retardation of growth, and the left kidney was in normal position. As recorded in the literature, 10 of 20 girls died on whom adrenalectomy was performed for this syndrome. All the recovered patients were operated on after the development of potent extracts of adrenal cortex.

PALMER, Philadelphia.

THE EFFECT OF SALTS ON THE DIABETES INSIPIDUS FOLLOWING POSTHYPOPHYSECTOMY IN THE RAT. H. G. SWANN and B. J. PENNER, Endocrinology **24**:253 (Feb.) 1939.

Swann and Penner report on the effects of sodium chloride, sodium citrate, sodium bicarbonate, sodium sulfate, potassium chloride, calcium chloride and Ringer's solution on experimental diabetes insipidus in the rat. The posterior lobe of the hypophysis, including the pars nervosa and pars intermedia, was removed. Control rats were subjected to a sham operation. The test period was of three weeks' duration. Sodium chloride in all concentrations aggravated the diabetes insipidus, and high concentrations (1.8 per cent solutions) were fatal in 6 of 7 rats in one week. Recovery from the aggravation caused by the solution of sodium chloride was immediate. Sodium chloride also prevented spontaneous recovery from operative diabetes insipidus in the rat. Ringer's solution and sodium bicarbonate were similarly diuretic. Sodium sulfate, sodium citrate, potassium chloride and calcium chloride exerted no diuretic effects. Solution of posterior pituitary given by injections prevented saline diuresis. The authors suggest that the remissions in diabetes insipidus observed in the presence of fevers and other illnesses or during fasting may be due to the low intake of sodium chloride.

PALMER, Philadelphia.

IODINE IN PITUITARY AND SOME OTHER TISSUES. EMIL J. BAUMANN and NANNETTE METZGER, J. Biol. Chem. **127**:111, 1939.

According to the analyses of Baumann and Metzger, the pituitary gland contains no more iodine than the ovary, testis, kidney, spleen or blood. Apparent high concentrations of iodine may be due to administration of iodine.

PAGE, Indianapolis.

TRANSFRONTAL HYPOPHYSECTOMY IN CASES OF ACROMEGALY WITH DIABETES. G. M. FASIANI, G. B. BELLOIN and M. QUARTI, Rassegna di neurol. vegetativa **1**:18, 1938.

The authors report a case in which there were classic signs of acromegaly for seven years, polyuria, with a urinary output as high as 9,700 cc. daily, and glyco-

suria, with the sugar up to 546 Gm. daily. At operation the infundibular region was gray and edematous. The tumor, an eosinophilic adenoma, was enclosed in the sella; an unstated amount was removed. There was an increase in the diuresis and glycosuria after operation. The latter then declined to approximately normal limits within two months; the former reached its original level. Roentgenotherapy was unavailing.

PUTNAM, Boston.

Diagnostic Methods

TONIC NECK REFLEXES IN CHILDREN. RANDOLPH K. BYERS, Am. J. Dis. Child. **55**:696 (April) 1938.

Byers discusses a series of cases in which various types of cerebral lesions caused marked changes in the normal reflex status. In discussing these changes in detail, he comments on the significance of tonic neck reflexes acting on the extremities in man as follows: "The occurrence in man of tonic reflexes of the sort under discussion, that is, those expressed by increase in extensor tone on the chin side and decrease on the occipital side, is an expression of the release of a phylogenetically and ontogenetically archaic motor mechanism from control by the newer superimposed mechanisms ordinarily present in the forebrain." He cites Minkowski as stating that modified postural changes in human fetuses may be controlled by the position of the head in relation to the body. Under proper conditions most babies up to the age of 3 months show classic passive tonic neck reflexes, and fragments of the pattern are seen if one watches their spontaneous postures.

Byers concludes from his studies that when children of over 5 or 6 years have fixed or progressive lesions of the nervous system tonic neck reflexes acting on the extremities are of serious prognostic significance and indicate a basic physiologic equipment so inadequate that no form of physical therapy has any real effect on the patient's disabilities. He calls attention to the fact that the patterns tend to change as growth advances. He believes that the importance of his work lies in the fact that the tonic neck reflex is of value as evidence of the extensive nature of cerebral lesions in infants and that it may be of value in identifying older children who are not likely to respond to therapy or to progress under an educational routine.

WAGGONER, Ann Arbor, Mich.

FALSE-POSITIVE WASSERMANNS IN CEREBROSPINAL FLUID. A. J. MCLEAN and I. C. MUNGER JR., West. J. Surg. **46**:455 (Sept.) 1938.

McLean and Munger's interest in the circumstances of falsely positive Wassermann reactions was aroused almost a decade ago by a case of craniopharyngioma in which, on the basis of a single determination of an indisputably positive Wassermann reaction of the spinal fluid with negative reaction of the blood, prolonged arsphenamine treatment had been given elsewhere, despite progressive disabling and localizing intracranial signs. The Wassermann reactions of the spinal fluid and blood were negative when successful operation was done on the tumor. Because fluid from the craniopharyngioma usually contains abundant macroscopically visible cholesterol crystals, the assumption was currently made that such extravasated fluid might be the cause of the falsely positive Wassermann reaction. Further cases have since been sought, and 10 are reported (instances of encephalomalacic atrophy, trauma, cerebrospinal rhinorrhea, electrical burn and neuritis). In most of these the common factor appears to be destruction or degradation of neuroprotein and neurolipid in areas in which cerebrospinal fluid stasis occurs—the function of the latter in these circumstances being merely to allow concentration of a reagent otherwise minimally present. The three most likely possibilities as to the nature of this unknown reagent are: 1. A globulin reagin truly analogous to syphilitic reagin may be elaborted directly during the degradation of neuroprotein. 2. Although the role of phanerosed cholesterol appears innocent

from the authors' experiments, other neurolipids of degradation (abnormal split products) present in such cerebrospinal fluid may combine with test antigen so as to sensitize the latter far beyond its usual titer and thus give rise to falsely positive reactions. 3. The mere presence of increased nonspecific protein produced during the degradation may, as in serum, offer such physicochemical inhibition of the usual measured dose of added complement for spinal fluid in routine tests that a falsely positive reaction would result. The minimum of laboratory work on any sample of spinal fluid should include a cell count, differential count and globulin, total protein, Kolmer and Lange tests. If the diagnosis indicated by laboratory tests is not in accord with the clinical observations, more fluid should be obtained and the tests should be repeated by two laboratories; the Wassermann-Kolmer test should then be made on spinal fluid with and without preliminary inactivation, and the result should be checked by flocculation concentration tests. If the laboratory results still disagree with the clinical facts, the tests should be repeated in three or four weeks; if the reaction is still positive, specific antisyphilitic therapy should be tried, though not before this.

EDITOR'S ABSTRACT.

REFLEX RELATION BETWEEN THE VISCERA AND THE SWEAT GLANDS AND ITS SIGNIFICANCE IN DISEASES OF THE INTERNAL ORGANS: THE VISCEROSUDORAL REFLEX. L. GUTTMANN, Confinia neurol. **1**:296, 1938.

Guttmann tested the sweat secretion in 3 cases of disease of the gallbladder and found in all cases a disturbance in sweating in the seventh to the ninth thoracic dermatome. He states that this circumscribed disturbance in sweat secretion is the result of a viscerosudoral reflex, which may be manifested as hyperhidrosis, hypohidrosis or anhidrosis. The sensory impulses, originating in the gallbladder, enter the spinal cord by way of the posterior roots and stimulate the corresponding vegetative nuclei in the lateral horn or in the intermediary zone, and the functional state of the sweat glands is altered, by way of either the rami communicantes or the efferent fibers in the posterior roots. Guttmann believes that examination of the sweat secretion may be of more value in determining the segmental supply of the viscera than the determination of Head's zones by sensory examination, as the former is independent of the subjective statement of the patient. Further observations should show whether this method may be used in the differential diagnosis of diseases of the internal organs.

DE JONG, Ann Arbor, Mich.

CEREBRAL ANGIOGRAPHY BY DIRECT INJECTION OF COMMON CAROTID. F. TURNBULL, Confinia neurol. **1**:344, 1938.

Turnbull describes a technic for cerebral angiography which is carried out by the direct injection of colloidal thorium dioxide into the common carotid artery, without an open operation on the neck. By this means satisfactory roentgenograms of the intracranial vascular tree, both arterial and venous, can usually be obtained. It is not an infallible method, but its use does not prejudice the success of subsequent operative injection, should this be necessary. Filling the external as well as the internal carotid circulatory system provides a minor source of difficulty in the interpretation of the plates. Prolonged pressure over the common carotid artery may cause profound alterations in an abnormal intracranial circulation.

DE JONG, Ann Arbor, Mich.

Society Transactions

ILLINOIS PSYCHIATRIC SOCIETY

H. Douglas Singer, M.D., F.R.C.P., *President, in the Chair*

First Regular Meeting, Jan. 5, 1939

Psychosis and the Central Autonomic Nervous System. Dr. H. Douglas Singer.

As I have stated in a previous article (Psychosis and the Central Autonomic Nervous System, *J. A. M. A.* **110**:2048 [June 18] 1938), I believe that in any psychiatric study it is essential to distinguish between the fact and the form of a mental illness. The fact of illness depends on the etiologic agent; the form of illness on the habits of adjustment peculiar to the person who is ill. Mental illness may be caused by: (1) problems of adjustment to the facts of the situation in which the person is placed—problems arising because (*a*) the person's endowment with the means for adjustment is inadequate, (*b*) training in the use of the means available has been inadequate or faulty or (*c*) there is a combination of the two preceding factors. Fundamentally, this group of illnesses is brought about by relations between the organism, with its existing constitutional endowment, and situations outside the organism. (2) Disturbances, of the nature of disease processes, within the organism itself, specifically, within the central integrating mechanisms of the nervous system. I have suggested also that the illnesses in the first group include what are known as psychoneuroses; the term psychosis, on the other hand, should be reserved for illnesses in the second group. If this definition is adopted, the term "functional" psychosis is a misnomer. Every psychosis is due essentially to some damage, reversible or irreversible, in the structure or function of the cells of the nervous system.

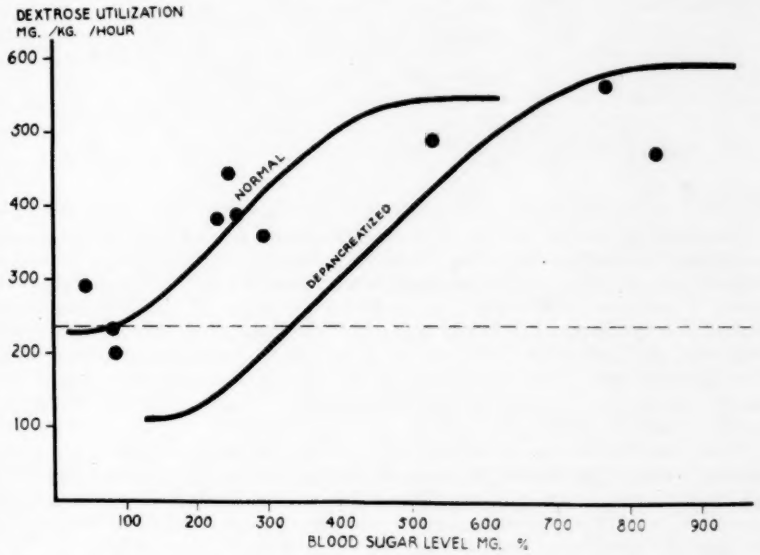
It seems worth while also to distinguish between damage of the two main integrating systems, the autonomic and the corticospinal. One constant characteristic of a psychosis as here defined is disturbance in energy of action. With this may or may not be combined evidences of interference with corticospinal nerve pathways, depending on the distribution of the lesions. The energy of reaction is integrated through the autonomic system; the form of reaction, including the conscious content—the manifest behavior—which may be activated either through the sensory projection pathways or through the autonomic system, is integrated by the corticospinal nervous system. Dementia paralytica is an excellent example of a disease process which presents varying combinations of disorder in both systems; always there is damage in the corticospinal neurons, giving rise to such symptoms as are expressed in the term dementia, which I do not regard as a psychosis. In about one half of the cases there is also a psychosis, or disturbance in the integration of energy. This implies that a psychosis means damage in the central, or highest, level of the autonomic system—not necessarily in the hypothalamus, in the case of damage to which there should be other localizing signs, but more frequently in the associative connections between the autonomic system and the corticospinal neurons of the cortex cerebri. There is now available a large mass of data concerning disturbances in autonomic functions in many different forms of psychotic illness which tend to support this view.

It should be stressed that the views here expressed do not in any way militate against the so-called dynamic interpretations of the meaning of behavior manifested, even in a psychosis. Why one person with a disorder in regulation of energy reacts with behavior of the overt, or manic-depressive, type and another, under conditions of a similar disturbance, with that of a covert, or schizophrenic,

type depends not on the nature of the illness but on the personality of the person who is ill. In the psychoneuroses, analysis of the personality and the situation—dynamic interpretation—is the only clue to the nature of the illness and the nature of therapy indicated. It seems evident that for a rational therapy it is essential to make some such distinction as that outlined. Experience with the shock methods and discovery of the physiologic means through which they operate should go far to elucidate underlying, and at present unknown, intraorganismal factors responsible for the psychoses.

PHYSIOLOGIC ACTION OF INSULIN IN SHOCK THERAPY. DR. SAMUEL SOSKIN.

It was formerly thought that the presence of insulin is essential for storage of glycogen and utilization of carbohydrate. Recent work has shown that these metabolic functions proceed in the completely depancreatized animal, in which insulin is entirely absent, although at slower rates than in the normal animal. Furthermore, in both normal and depancreatized animals the rate at which sugar is utilized depends on the height of the blood sugar level. However, the presence of insulin in the normal animal enables it to maintain at a low (normal) blood sugar level that rate of carbohydrate utilization for which the diabetic animal



The smooth curves (Soskin, S., and Levine, R.: A Relationship Between the Blood Sugar Level and the Rate of Sugar Utilization, Affecting the Theories of Diabetes, *Am. J. Physiol.* **120**:761, 1937) represent the relationship between the height of the blood sugar level and the rate of carbohydrate utilization in the presence of insulin (normal dogs) and in the absence of insulin (depancreatized dogs). The horizontal broken line indicates the rate of utilization of sugar in normal dogs at their normal blood sugar levels. The point at which this line crosses the curve for the depancreatized animals indicates that the latter exhibit the normal rate of sugar utilization when their blood sugar levels are within the range of 300 to 400 mg. per hundred cubic centimeters, characteristic of untreated diabetes. Each black dot represents an experimental result (Soskin, S., and Levine, R.: On the Mode of Action of Insulin, *Am. J. Physiol.* **123**:192, 1938) for a different dog, when given an injection of insulin at a particular level of the blood sugar. The additional insulin causes no increase in utilization of carbohydrate above that of the untreated normal animals.

requires hyperglycemic levels. This and other evidence indicates that insulin may be regarded as a catalyst which affects some phase of metabolism preceding the entry of sugar into the tissue cells for storage or oxidation. From this point of view it is not surprising that evidence is also forthcoming to show that the normal animal has an optimal supply of insulin for the maximal catalytic effect and that the administration of additional insulin causes no increase in utilization of carbohydrate at any given level of the blood sugar. Thus, the exposure of nondiabetic tissues to supernormal concentrations of insulin cannot be regarded as having any stimulating or beneficial effect on carbohydrate metabolism.

The experimental evidence which has been cited relates chiefly to carbohydrate metabolism in muscle. However, a similar relation between the blood sugar level and utilization of sugar has also been shown to hold for the nerve tissues of the brain, in dogs and in man. The lower plateau, in the S-shaped curve which expresses the relation of the blood sugar level to utilization of sugar indicates that the latter cannot be depressed below a certain minimal rate by any degree of hypoglycemia. Marked hypoglycemias may therefore drive the available supply of sugar from the blood, below the minimal requirements of the tissues. Under such circumstances the muscle may have recourse to its stored glycogen, or may perhaps turn to protein or fat as a source of energy. It is generally agreed, however, that nerve tissue has little stored carbohydrate and cannot utilize protein or fat. It follows that the nerve tissues during marked hypoglycemia are unable to maintain even the minimal rate of metabolism compatible with their well-being. This explains the recent reports that prolonged insulin hypoglycemia has led to irreversible damage to the central nervous system in experimental animals, and to similar pathologic changes and mental deterioration in schizophrenic patients. It may be concluded that insulin "shock" therapy has been well named!

PHYSIOLOGIC STUDIES OF "SHOCK THERAPY." DR. ERNST GELLHORN (by invitation).

Experiments carried out during the past three years in collaboration with Glickman, Moldavsky, Ingraham, Yesinick, Domm, Kraines and Darrow are reported. A synergistic action of hypoglycemia and anoxia on the central nervous system of man and animals is demonstrated. Furthermore, simultaneous records of the blood pressure, the galvanic reflex and responses from the nictitating membranes and pupils show that metrazol in convulsive and subconvulsive doses stimulates predominantly the sympathetic nervous system, leading to spontaneous sympathetic discharges and increased sympathetic responses to a standardized sensory stimulus.

Insulin hypoglycemia and metrazol convulsions appear to stimulate the sympathetic division of the autonomic nervous system. There is a fundamenal difference between the action of metrazol and that of epinephrine, in that epinephrine decreases the reflex responses of the sympathetic system whereas metrazol has the opposite effect.

The significance of these findings for the treatment of schizophrenia is discussed (Gellhorn, E.: Effect of Hypoglycemia and Anoxia on the Central Nervous System: Basis for Rational Therapy of Schizophrenia, ARCH. NEUROL. & PSYCHIAT. **40**:125 [July] 1938).

MECHANISMS OF ACTION OF "SHOCK THERAPIES." DR. R. W. GERARD (by invitation).

The action of various "somatic" therapies in the treatment of schizophrenia can be rationalized only after considering several basic questions about the disease: 1. Is there a somatic lesion, or is the disturbance solely at the "psychic" level? 2. If some anatomic or physiologic disturbance of the nervous system exists, can it be localized, and to what part? 3. What is the nature of this lesion? A fourth question, though important to a final understanding of the disease, need not be considered in evaluating shock therapy: What is the pathogenesis of the lesion?

The first question, if answered negatively, would automatically throw the interpretation of successful shock therapy into the psychologic realm as an effect

of "mental" shock. Present psychiatric opinion seems to accept the existence of both somatic and psychic factors in mental disease, with certain groups of disorders falling overwhelmingly into the somatic and others into the psychic categories, but with most somewhere between. Certainly, large numbers of schizophrenic persons manifest, in addition to the mental phenomena, a considerable number of bodily disturbances, such as catatonia, high skin resistance, low blood pressure, disturbed sugar tolerance and low basal metabolism, so that malfunctioning of the nervous system is evident at the somatic level. Further discussion, then, is intended to apply to such cases as those in which there is a definite "lesion," without insisting that this is true for all, or even the majority.

As to the location of the disturbance, one thing is clear: The behavioral abnormalities that lead to a diagnosis of mental disease are the results of malfunction of the cerebral cortex. What is not so obvious is whether this cortical machinery is locally injured, for example, by abnormal oxidative metabolism of cortical neurons, or whether it is itself intact but is driven erratically by other neural mechanisms in which is seated the disturbance, of which the diencephalon and autonomic nervous system have been emphasized. All parts of the nervous system, autonomic and central, neuraxial and suprasegmental, so intimately play on one another that abnormal functioning of any one part does not indicate that it is the primary offender. On the other hand, if, for example, hypoactivity of the orthosympathetic system is considered primary, it is still essential to a complete interpretation that the way in which this hypotonia deranges cortical function be also adequately explained.

The third question, the nature of the disturbance, is, in several aspects, the most susceptible to answer at present. Anatomic degeneration of neurons is not necessary to the schizophrenic state and, indeed, cannot be too extensive, else functional restoration would not be possible. Aside from actual destruction, abnormal functioning of neurons can result when the normal activity is diminished, exaggerated or disordered (loss of normal integrated behavior patterns of groups of neurons). Depression and disorganization of neuronal function tend to vary together in physiologic experiments, as if under control of the same factors, and the disease symptoms are likewise understandable in terms of diminished neural activity and integration.

Considered broadly, "hypotonicity" in action and discharges of nerve cells must be due to one of three factors: (1) abnormal influx of nerve impulses (decreased excitation or excessive inhibition); (2) an abnormal physicochemical milieu in the surrounding tissue fluid and blood (decreased potassium, lowered temperature or hypoxia), or (3) an abnormal metabolic system within the cell (decreased content of enzymes or intermediates). A combination of any or all of these may be important in schizophrenia, and it is at present impossible to decide whether the diminished cortical activity is a direct consequence of decreased autonomic activity (or conversely, the cause of it), or of a metabolic defect in the cortical cells themselves.

Certainly, much factual material previously summarized (Gerard, R. W.: Anoxia and Neural Metabolism, ARCH. NEUROL. & PSYCHIAT. **40**:985 [Nov.] 1938) makes an impressive case for disturbance of oxidation in cortical neurons, and the arguments for sympathetic disturbance have been well presented by Dr. Gellhorn. All the nonpsychologic therapies of the psychoses for which good results have been claimed have in common the evocation, immediately or by rebound, of increased respiration in the brain. Hypoglycemia, hypoxia, metrazol, thyroid, *Dauerschlaf*, hyperthermia and carbon dioxide all modify the oxidation of dextrose by the cortex.

Since many of these methods also increase autonomic activity, it remains for future tests, such as those with vital dyes, which accelerate respiration (some promising results with pyocyanine are already at hand), to help in differentiating the possible mechanisms of their therapeutic action. Meanwhile, such a physiologic analysis of the problem is of real value in that it suggests experiments to determine the mechanism of action of the now popular therapies and points to other agents for therapeutic trial.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND THE NEW YORK NEUROLOGICAL SOCIETY

MORRIS GROSSMAN, M.D., *Chairman of the Section, in the Chair*

Joint Meeting, Jan. 10, 1939

THE TREATMENT OF DEPERSONALIZATION. DR. PAUL SCHILDER.

The picture of depersonalization is that of a well circumscribed chronic neurotic condition which offers great difficulties for psychotherapy. However, by psychoanalysis or methods akin to this good results can be obtained if the treatment is continued for years.

In the series of cases reported, treatment with mescaline and benzedrine was ineffective. In 9 cases intravenous injections of metrazol gave good results. However, in some improvement was incomplete. This treatment should be combined with psychotherapy.

The effects of treatment are probably due to organic factors. The psychologic factors alone are not sufficient to explain the results.

Metrazol is effective in treatment not only of schizophrenia but also of manic-depressive psychoses and specific types of chronic neurosis. The question arises whether other types of so-called psychogenic disturbances (neuroses) will be helped by this treatment.

DISCUSSION

DR. MANFRED SAKEL (by invitation): I was interested in the paper of Dr. Schilder. I consider it an important step in the endeavor to treat neuroses somatically. I do not dare to discuss the psychologic aspects of the depersonalization, since Dr. Schilder is one of the most experienced in this matter. It may be that I shall disappoint those who expect me to defend only the somatic point of view.

Nevertheless, I take the liberty to make some general remarks. Depersonalization should be considered as a kind of dysfunction in the perception of one's own personality. This definition in itself brings up a difficult question. To discuss the problems of description would force me to define the term "personality" itself. I do not want to involve myself in these far reaching questions. I shall call attention only to the fact that there are symptoms in many other diseases which could easily fit into this group. There are diseases generally assumed not to be derived from psychologic sources alone. I should like to emphasize that symptoms similar to those described by Dr. Schilder are experienced by the schizophrenic patient at the onset of his illness. The external world often seems strange to him, and the surrounding environment means something different than before. He perceives peculiar, quaint features, both without and within, which he did not notice before.

It seems to me that the normal picture of the world and the feeling of being familiar with it, as well as the feeling of being familiar with one's own psychologic condition, should be considered always as bound to normal functions of the brain. It seems, too, that every change in the organism, especially that in the functioning of the brain, is perceived in some manner by the self. I can imagine it as a kind of switchboard on which the red lights flash up only when disturbances occur, to indicate them to one's perception. Normally the functioning is not perceived at all, because no red light flashes.

These warning signs may come from two sources: from the pathways of perception, if confused and short circuited, resulting in hallucinations, and, second, from the disturbance of self perception. These experiences are both expressions of dysfunction of the brain. This does not mean that dysfunction cannot be induced by psychologic causes. It is often so induced. I recall the familiar example of the cat which shows stormy intestinal movements when stroked in

the wrong direction. Every one will admit that these movements are at least induced by biochemical stimulation and, too, that the releasing cause is the feeling of unpleasantness. The elimination of this result could be achieved from both the biochemical and the psychologic poles.

I may stress that in some cases of neuroses there is a special preparedness for biochemical dysfunctions. A slight cause, psychologic too, is sufficient to release the symptoms. Dr. Schilder pointed out at the end of his paper that somatic changes are finally and basically responsible for neurotic symptoms. I am pleased to say that it is the point on which I agree with him in general.

May I add that at the beginning of the pharmacologic shock therapy of psychoses I treated a great number of patients with almost all diseases within the psychiatric range? It happened that among these, I treated several patients with symptoms of depersonalization. The results were most satisfactory. I confess that I did not publish the results, being afraid of the accusation of having a cure-all method. I regret that Dr. Schilder had not the opportunity to watch the development of this treatment from the beginning.

I treated in the usual way persons with obsessional neuroses, as well as patients with symptoms described in a paper by Dr. Schilder. To provoke the imminent convulsion during hypoglycemia, I used metrazol about two or three hours after the administration of insulin. The terrifying effect of the preconvulsion was eliminated. None of the patients feared the treatment or interrupted it, but this is only a minor point. I should like to point out chiefly that in quality and in duration the effect of applying the entire treatment as I originally described was much better.

For these patients the dose of metrazol required to provoke a convulsion during the hypoglycemia averaged about one-third that which Dr. Schilder mentioned. Some patients who did not have symptoms of depersonalization during the illness showed them in a marked degree for a short time after awakening from the coma. For example, a patient with an obsessional neurosis, as well as one with schizophrenia, experienced these symptoms. I did not keep records of the duration of improvement in cases of neuroses, so I cannot say much about it. However, in the cases of 2 patients whom I treated in the manner described I heard that the improvement continued for two years. One patient was a business executive who had been compelled to neglect his business for a few years because of illness. After treatment he was able to resume work, with full responsibility and, as I was told, with success. He was still doing so when I last heard of him.

DR. LOUIS WENDER: Since Dr. Schilder's paper deals with the treatment of depersonalization, I shall not enter into the psychodynamics of this disorder and its treatment by psychotherapeutic means alone. No doubt there are underlying psychologic factors in this symptom complex. Depersonalization, per se, is not a disease entity but a symptom prevalent in many mental disorders. It is common in schizophrenia and manic-depressive psychoses and also in chronic psychoneuroses. Although patients may describe their symptoms somewhat differently, the concurrent syndrome is that the outer world seems strange, that there is a feeling of unreality and estrangement from the external world. There is a loss of "feeling tone." This symptom is so common among hospital patients with functional disorders that one is at a loss, at times, to know how to overcome it, even with intensive psychotherapy. Dr. Schilder tonight has demonstrated that depersonalization, whether as a symptom alone or associated with other symptoms of mental disease, can be overcome by the use of chemotherapy.

At the Hastings Hillside Hospital my associates and I have had the same experience with metrazol as that reported by Dr. Schilder. We have administered metrazol to 43 patients and have completed the course with 36. Twenty-one of these patients were suffering from chronic psychoneuroses and depressions in which the depersonalization syndrome was marked. Of the 15 others manifesting a schizophrenic reaction, only a few presented any symptoms of depersonalization.

Our results were satisfactory. As a matter of fact, we are of the opinion that in cases of depression in which the stupor is not deep, when there is no retardation but symptoms of depersonalization and a feeling of unreality are marked, metrazol has a beneficial effect in accelerating the rate of recovery. The common statement that depressions disappear anyway, even without chemotherapy, is probably true, but metrazol precipitates an earlier recovery and perhaps breaks up the manic-depressive cycle. I make this statement on the basis of experience with 2 patients, both of whom had manic-depressive psychoses—1 with obsessional thinking and 1 with a depersonalization syndrome. The latter had had two previous attacks, each lasting about a year; the other had also previously been sick for about nine months. In each case the depression was followed by a hypomanic phase. Both patients recently had a recurrence of the episodes and were hospitalized; metrazol was given to each. Both recovered rapidly, the duration of hospitalization in 1 case being seven weeks and in the other about ten weeks. One patient left the hospital in July and the other in September; neither showed subsequent hypomanic reactions, and both are doing well at present. This, of course, requires further study and verification.

I am in agreement with Dr. Schilder that metrazol and insulin are not the only remedies in treatment of the chronic psychoneuroses; that such persons require psychotherapy and that the psychotherapy should be started as soon as the patient begins to show response to chemotherapy; that, furthermore, the administration of metrazol should not be discontinued suddenly, but should be reduced gradually. On the basis of our experience at Hastings, after the patient begins to show definite improvement the treatment is reduced at first from three times to twice a week and later to once a week, the patient in the meantime receiving intensive psychotherapy. After the injections are completely discontinued, active psychotherapy is continued until the patient is discharged. We believe that this prevents recurrence of the mental disorder. So far, none of our patients in the group that received metrazol and recovered or showed improvement has returned to the hospital.

How metrazol works I am unable to state. Personally, I do not think the mechanism is a fear phenomenon, for our experience has shown that if the patient does not have a definite convulsion he does not show the proper response, and that the patient's fear when there is no convulsion is much greater than when he has a seizure. As a matter of fact, if there is no convulsion the fear of impending death is so marked that the patient sometimes refuses to have another injection unless he is promised that the dose will be large enough to give him a convulsive seizure. Repeated injections without convulsions do not produce any change. On the other hand, if there is going to be improvement, it can be noted after the third or fourth consecutive convulsion. Therefore, if fear is the cause of the reaction it probably touches the deep unconscious; certainly, it is not a conscious fear that causes recovery. The probabilities are that the metrazol seizures disturb the biochemical relations in the system, perhaps discharging certain toxins and reorganizing the cortical function.

Our experience has also shown that metrazol can be used in treatment of severe chronic psychoneuroses, especially of the obsessional type, or the chronic anxieties. At present, we have a patient with a severe compulsion neurosis of three years' duration, who prior to coming to Hastings received psychoanalytic treatment for ten months and was just able to get along. When admitted to the hospital he was so full of obsessions and compulsions that it took him hours to dress and undress. It would take him a half-hour to wash his hands. He was afraid to touch anything, and even to say anything, because he thought that his words might hurt some one. He was so obsessed that he felt that even his presence might hurt people, and, as a result, stayed in his room for hours at a time before he could decide to go out. When the family wanted him to go out of the house they resorted on several occasions to putting a strong disinfectant in his room, in order to choke him out. This patient received eighteen injections of metrazol; by the time he had had the twelfth injection we noted a change in his

condition. Practically all the obsessions enumerated have disappeared; he cleans around the hospital, uses his hands freely and enters readily into conversation. He is at present under active psychotherapy in order to remove some of the more deeply underlying mechanisms, in the hope that we may change his character of thinking.

There are many patients whose financial status does not allow them the luxury of psychoanalysis for a year or two in the hope of having their difficulties adjusted, and there are also many persons whose intellectual makeup is such that even if they can afford the treatment, analysis is of no avail. We who practice among the former group have to resort to various means of therapy. If metrazol can remove the symptoms and make a patient a useful member of his social group, it should be tried for all those who fail to respond to psychotherapy or in whom the duration of the illness is over a year.

DR. C. P. OBERNDORF: I welcome Dr. Schilder's experiment in trying to influence by metrazol the course of this extremely stubborn disorder. There seems to be a legitimate reason for this procedure; first, that in more than half the patients with depersonalization with whom I have worked intensively the disease would be called schizophrenia, a condition in which metrazol often produces striking beneficial results; second, that the results with psychoanalysis, as Dr. Schilder has pointed out, have been unsatisfactory in many cases. Two patients treated by psychoanalysis, I am happy to say, are well after a relatively short time, a year and a half, and have remained well for over three or four years. However, another patient, after possibly two hundred hours of treatment with analyst A, two hundred hours with analyst B and possibly one thousand hours at my hands, is still very ill. She says that as soon as she has some grasp of the pathologic situation she must revert to her other self. She said: "Some people stay in the world and go insane. I retire from it, into my other self, and have stayed sane." By all criteria of external adaptation she is sane. The second self operated a large mill efficiently and steadily, but what she called her real self, her true self, she described as existing only as a faintly glowing ember.

Without going into the debatable question of feminine pulchritude, I should say that the fact that the patients I have in mind differed so strongly in their histories from Dr. Schilder's corroborates what many authors have pointed out, that little uniformity is established in the disorder called depersonalization. It is difficult to determine from the brief clinical material Dr. Schilder has presented whether the cases are pronounced instances of depersonalization or cases in which symptoms of unreality occur in the course of other psychiatric syndromes.

I wish to say that freudian psychology is generally on a horizontal level, with layers of the conscious, foreconscious and unconscious. In addition to considering thought processes as occurring on a horizontal plane, one may also think of them as occurring in perpendicular planes. One may even picture thought as occurring in irregular currents, with depth as well as direction. Through some psychic trauma, the stream of thought may be thrown into a whirl, perhaps similar to the whirl which occurs in a flowing stream of water above submerged rocks. Such a thought whirl becomes separated from the main stream, and a mass of such whirls may cause an impasse of thought. Thus, the patient is able to operate efficiently and conduct himself normally through use of the thoughts which are not drawn into the whirl. That part of the patient's psychic life which is included in the whirl goes actively round and round, without ever joining the main stream.

It appears that shock, whether it is induced by metrazol, or, as Dr. Freeman of Washington has mentioned, through lobotomy, or through mechanical force, such as a blow, has the effect of temporarily changing this flow. I refer particularly to currents of thought flow which have become centered around traumatic psychic situations and have been unable to regain the progressive thought currents.

All the speakers have mentioned that metrazol must be followed by psychotherapy. Just what form this psychotherapy is to take is necessarily undetermined at present. Perhaps as time and experience unveil the effective mediums for

changing the speed, direction and intensity of flow of the thought current, the need for all psychotherapy will be lessened.

DR. PAUL SCHILDER: I am grateful for the discussion, and I am glad that the views of the discussers agree so closely with mine. Dr. Sakel has justly mentioned that depersonalization can be observed also during awakening from insulin coma. One of my observations is identical. One could make some interesting speculations about this fact, especially when one considers that depersonalization has also been observed after epileptic attacks. However, I have brought this paper before the society chiefly for practical reasons. Although one of my patients has now been completely cured for more than ten months, much more work will be necessary in order to appreciate the value of shock therapy in depersonalization and neuroses in general. Such work needs the cooperative effort of a large number of observers.

A METHOD FOR DIFFERENTIATING MANIC-DEPRESSIVE DEPRESSIONS FROM OTHER DEPRESSIONS BY MEANS OF PAROTID SECRETIONS. DRS. EDWARD I. STRONGIN and LELAND E. HINSIE.

In a previous report, it was shown that the secretory rate of the parotid gland in manic-depressive depressions is lower than the lowest value for the "average normal" person. In the present investigation we set out to determine whether this low rate is found in all types of depressions or whether it is characteristic of the manic-depressive depressions. The findings can be summarized as follows:

1. Determinations of the secretion of the parotid gland were made in a series of cases of undifferentiated depressions before they were studied clinically. If the readings were below an average of 0.01 cc. per five minutes during a test of a half-hour's duration, the case was recorded tentatively in the experimental records as one of manic-depressive depression. If the average reading was above 0.01 cc. per five minutes, the case was recorded as not one of manic-depressive depression. No other differentiation was attempted. The results were then filed for comparison with the clinical diagnosis.

2. The clinical diagnosis in each instance was later made by two psychiatrists, working independently. The diagnoses of the two psychiatrists were then compared. When an agreement on the diagnosis occurred, the case was included for report in this communication. If any disagreement or uncertainty occurred it was believed that the condition was not yet sufficiently clearcut to warrant inclusion in the group. These clinical diagnoses were then compared with the laboratory diagnoses based on the parotid secretory rate.

3. It was found that the laboratory diagnoses based on determinations of the secretion of the parotid gland agreed with the clinical diagnoses in 40 of 43 cases. Specifically, in 21 of 23 cases of clinically determined manic-depressive depressions the parotid index was in agreement. In 19 of 20 other cases of depressions not diagnosed as manic-depressive the parotid index agreed, the secretory test indicating merely that the depression was not manic-depressive, with no attempt further to differentiate them.

4. The secretory rate of the parotid gland was inhibited in the earliest stages of the disorder, before it was possible to make a definite diagnosis of manic-depressive depression by the usual psychiatric procedures.

5. The secretory inhibition remained during the daily fluctuations in mood of the patient, but the rate returned to the normal range when the patient recovered from the depression.

6. The rise of the secretory rate when the depression left might be sudden.

7. The parotid secretory test can be made within an hour with simple, inexpensive apparatus, based on a modification of the Lashley suction disk and involving little technical training.

DISCUSSION

DR. KARL M. BOWMAN: All will agree that any simple test for the differential diagnosis of one of the functional types of mental disease would be a valuable

contribution. At present much confusion exists in the method of classifying depressions. Kraepelin brought together a group of disorders which had been previously thought of as dissimilar and labeled them manic-depressive insanity. However, Kraepelin kept a certain type of depression out of the manic-depressive group, labeling it involutional melancholia. Recently, the classification has been altered to place among the psychoneuroses a certain type of depression which has been labeled reactive depression. At this time there is a great deal of disagreement among psychiatrists as to whether the present classification of depressions is correct. Some psychiatrists believe there is no such disease as involutional melancholia and hold that in most cases the condition is really manic-depressive depression.

There is also considerable question as to whether the so-called reactive depressions are a form of psychoneurosis. The difficulties of differentiating between schizophrenia and manic-depressive psychosis are recognized by all psychiatrists, and it is admitted that there are many borderline cases in which there will be difference of opinion among the best psychiatrists. With all this in mind, it is of interest that Dr. Strongin and Dr. Hinsie have devised a simple test by means of which they have been able to differentiate between manic-depressive depression and depressions associated with other types of mental disorder. The material presented by the authors appears to be convincing, although, obviously, the number of cases is so small that further confirmatory work with a larger number must be done before one can consider that the authors have proved their point. Therefore, I am inclined to accept, subject to further study, their claim that they have devised a specific test which will enable one to determine more accurately whether a case is one of manic-depressive depression.

If this test is valid, it will enable one to be more precise in the concept of what constitutes a manic-depressive depression. One may compare this test with the Wassermann test for syphilis. Older writers in psychiatry made many mistakes in the diagnosis of dementia paralytica, and their description of the disease was incorrect at times because they were trying to diagnose a disorder for which they had no precise or final criteria. One now recognizes a different clinical picture of the disease from that given in the older descriptions. If there is available now a specific test for manic-depressive depressions one will be able to study this disorder in a much more satisfactory fashion because one will know what one is studying. I wish also to point out that the discovery of a slowing of the parotid secretion seems to be in agreement with what is known of most reactions occurring in manic-depressive depression. Many writers have described the slowing of various vegetative functions; so the findings cited seem to confirm the preexisting ideas.

It seems that this test, if valid, has certain specific values. It is of importance to know the type of depression during the early stages, for the treatment and the prognosis are dependent on the diagnosis.

Another point which seems of importance is that when a patient actually improves the results of the test are altered, but transitory improvements, which do not indicate an actual recovery, fail to make any alteration in the test. This should enable one to determine whether a patient has really improved sufficiently to be discharged, and should prevent one from discharging patients who are not really cured but who, superficially, may appear to be so.

The authors of this paper are to be congratulated in providing a specific test of this sort. I hope they will carry on their studies with other types of depressions, for I should expect that there may be specific changes of a different type, particularly in depressions which belong to the catatonic type of dementia praecox.

DR. HAROLD G. WOLFF: About a quarter of a century ago, Pavlov, in attempting to study some of the bodily changes that occur with mental functions, devised a method by which he could determine the salivary secretions. He took saliva because it was technically easy to collect and, owing to its fluid nature, easily measured. Later, in the United States, through Lashley and, now, through the

workers who have reported this evening, this method has been modified so that it may be applied to man. As pointed out by the authors of the paper, it is simple and accurate. They have found that in the group of patients with depression of the manic-depressive variety dryness of the mouth, with the accompanying complaints of bad taste and halitosis, can be expressed in quantitative terms. The other changes so common in this group of patients are, as Dr. Bowman indicated, loss of appetite, gastric hypomotility, constipation, changes in menstruation, loss of weight and a striking alteration in the sleep curve. Of all these, probably the salivary secretion is the most readily studied, and, as has been shown, it is so constant in its performance as to allow of a clinical grouping. I should like, and am anxious, to accept the criteria suggested as a basis of a diagnostic grouping. I have, however, two questions to put to the authors: Do all of this group of patients with manic-depressive depressions, whether deeply or less depressed, show a similarly low secretory rate? Second, the important group of depressed patients which cannot be decided on by the experts is the very group about which one would like to know most. It is that group in which the test would be most helpful, and perhaps the authors can state, since some time has elapsed, to what extent the salivary test was superior to the ordinary clinical data in formulating the nature of the psychoses?

Dr. Smith Ely Jelliffe: I have little to say beyond first offering a slight apology. Balzac—I believe it was—once wrote that when a man gets to be 70 he has learned so much that what he knows can only be expressed in the words of a crazy man. With such an excuse I would make my little offering. Both papers are of great interest because there is a correlation, a very close correlation, between them; as the time has gone by when I might have said something about the first paper, I shall consider both papers in my remarks.

As to the paper on parotid secretion: What is it that is being measured? It is not the nosologic conception. I believe that the writers are really dealing with the amount of energy related to the anxiety. In other words, the person with a definite manic-depressive depression is on the edge of the suicide impulse nearly all the time. Suicide means also its ambivalent murder, as Dr. Schilder has already pointed out. Murder is in the heart of the person who depersonalizes, and such a one would destroy the world by retreating from it by the mechanism of depersonalization. Hence the anxiety. Everybody knows how the mouth waters at the anticipation of something pleasant, and every one has had the experience of having a very dry mouth when called on to exercise a disagreeable or aggressive function. Anxiety thus arises. Dr. Schilder has pointed out that there is a sadomasochistic component in the phenomenon of depersonalization, and, further, that, as a symptom rather than as a syndrome, depersonalization is frequent in the depressed manic-depressive illness. The experiment on parotid secretion points to a constitutional factor. This is a factor of much significance and constitutes, as it were, the more malignant manic-depressive psychosis. Hence the value of the sign for both diagnosis and prognosis. The depersonalized person carries out, symbolically, the sadomasochistic impulse (kills and is killed) and thus escapes the anxiety that would otherwise bring about a real murder or a real suicide. This anxiety situation is the background of the parotid phenomenon.

Dr. Edward I. Strongin: There seems to be little relation from the secretory point of view between involutional melancholia and manic-depressive depression. The rate in involutional melancholia seems to be within the upper limits of the normal, while the secretory rate observed in the manic-depressive depression is below the lowest limits of the normal range. In reply to Dr. Wolff's question: "Do all patients, whether deeply or less depressed, show a similarly low secretory rate?" we can state that our present findings indicate this low secretory rate in both early and advanced depressions.

At the time that these secretory tests were made, most of the cases reported were in the "unclear" group; as the psychiatrists obtained a clearer picture of the case they were able to express a definite opinion. At this point these cases were removed from the "unclear" group and checked with the secretory findings,

which were definite at all times. However, the validity of the secretory findings could not be determined until the psychiatrists were able definitely to make a diagnosis in these cases.

DR. LELAND E. HINSIE: When Dr. Strongin first came to us about three years ago with the thought of doing work on the parotid secretion he had had several years of intensive experience in that field. We were pleased that he brought with him a method for investigating something that had always been of interest to psychiatrists in general. Psychiatrists had noted for years that psychiatric patients often showed changes in oral secretions, but no adequate method had been developed for investigating parotid secretions.

Although our interests have extended now over a period of approximately three years, during which time some interesting results have come about, we believe that it will be several years before we can speak with authority.

The paper this evening stressing the differentiation of depressions by the parotid secretory rate covers observations on 43 patients who were checked and rechecked several times from the clinical as well as from the laboratory point of view. We are impressed with the thought that our studies point to a method for distinguishing depressions of the manic-depressive order.

Dr. Strongin and I have made no special effort to postulate regarding the cause or causes behind the different secretory rates observed in our patients. Since this work is relatively new, we believed it more desirable to occupy ourselves with the gathering of overt facts. I think, however, that Dr. Jelliffe's suggestion may be reasonable. Emotional reactions do participate in somatic changes. It is reasonable to believe, as Dr. Jelliffe has indicated, that anxiety, or a mood akin to anxiety, may contribute in an important way to the changes in secretory rate, such as those observed. We believe also that the parotid secretory rate may represent more than mood. It may be a reflection of the state of the autonomic or vegetative apparatus. The parotid gland is known to have nerve supply from the sympathetic and from the parasympathetic nervous system. Whether the vegetative nervous system is simply a vehicle for the expression, in this instance, of parotid secretion is not known to us. Behind the vegetative apparatus may be both psychic and organic factors. What pleases us is the fact that through the study of parotid secretions in the manner in which we have been able to study them we are measuring something connected wiith the organism, and perhaps with the vegetative apparatus, in a direct manner. It is one of the few instances to date in which glandular activity may be directly measured.

PSYCHIATRIC DISORDERS IN FIFTY SCHOOL TEACHERS. DR. JAMES H. WALL, White Plains N. Y. (by invitation).

Psychiatric disorders are described in 50 women teachers who were patients in the New York Hospital, Westchester division, between 1920 and 1935. They were from different localities and from both public and private schools. The average age at the time of admission was 47. The study of this group corrects the impression on the part of psychiatrists and others that the prognosis in such cases is not good. One half of the patients recovered fully and were able to resume teaching with efficiency.

The family histories showed an incidence of mental illness in 29 of the patients. A stern, dictatorial type of father was common, and his influence was reflected in the prudish and inhibited traits of the patient's personality. The patients came from large families, and many of them were the eldest. They held a position of respect, and early in life began to take seriously their responsibilities. During their teens and twenties they had shown little or no interest in members of the opposite sex. The families of 37 of the patients were dependent on their earnings, a situation largely responsible for their choice of and continuation in the teaching profession. They were described as tense persons with few hobbies and without much ability to relax. Irregular hours of sleep and rest were observed. They were inclined to be hypochondriacal and to "shop" from one physician to another. The climacterium was a factor in the beginning of the illness of 34 of the patients.

There were 34 patients with agitated depressions, 14 with dementia praecox and 2 with manic attacks. Two illustrative case histories are presented. The common factor in the trend was the feeling on the part of the patients that they were confronted by instinctual urges which they were unable to accept or to manage. Associated with this state in the 34 who had agitated depressions were agitation, anxious depression and hypochondriacal notions. The same was true for a time of the 14 patients with dementia praecox, but projection became more manifest as the condition progressed. A similar conflict was seen in the 2 patients with manic attacks. The conflict was dramatically portrayed by a fear of burning and consuming fire in the trends of 20 of the patients. Suicidal tendencies were present in most of them.

Treatment at first was directed mainly toward securing rest, sleep and a proper state of nutrition. Prolonged baths, packs, hydrotherapy and massage were used to combat the restlessness and agitation. Although starting on a limited schedule, the majority of these patients were soon participating in a full program of occupational therapy, physical education and social activities. Psychotherapeutic interviews were frequent, and the intelligence and psychologic interest of the group contributed a great deal to the careful study and modification of their personality difficulties. The acquiring of a more tolerant attitude toward instinctual drives and problems was the most difficult to achieve, and the most helpful. Those who recovered were able to understand that they had turned aside or avoided inner needs without facing and making some sort of peace with them. In some instances the recovered patients spoke of their illnesses as an explosive release from a smoldering conflict of years' duration, as something which cleared the atmosphere. Some of these patients remarked, years after discharge, that after the illness they had seemed to function better than ever.

Many of them learned to play for the first time in their lives, having received instruction in many indoor and outdoor sports. Lasting hobbies were acquired in occupational therapy. Some placed great value on the benefit derived from close daily contact with members of their own age in the social and recreational side of their treatment. A better organization of their time for work, rest and sleep was stressed by some.

Twenty-five of the 50 patients recovered and were able to resume teaching. The other 25 did not return to work, and most them have been in hospitals for mental disease. The average hospital residence of those who recovered was twelve months. The average residence here for those who did not recover was ten months, with an average of eleven months for the entire group. The 14 patients with dementia praecox did not resume work. The 2 patients with manic reactions had subsequent attacks. The 9 patients who did not recover from the agitated depressions were persons with narrow, rigid personalities, and their trends and behavior displayed a prolonged, drawn-out battle in which instinctual gratifications, though in regressed expression and form, were a little stronger than the personality forces for normal adjustments.

Some indications in the way of prevention were suggested by the study. The family relations could have been managed differently. The narrowed interests and the failures to adopt and cultivate wholesome hobbies and recreations were remediable, particularly applicable to those who thought such adjustments could wait until the time to retire. The shifting philosophies and faiths and the "shopping" from one healing cult to another could have been modified. The earlier achieving of some solution and harmony out of the energy-consuming conflict between unfaced inner demands and too rigid ideals was possible. The importance of sufficient rest, relaxation and sleep has been stressed by some teachers who were interviewed after passing through the crises of their lives, including retirement, without a breakdown.

DISCUSSION

DR. ROBERT B. MCGRAW: On reading Dr. Walls' paper there came readily to mind a great many cases from private and from clinic practice in which the histories were strikingly similar to those cited.

I am interested to observe that, in referring to the family history, Dr. Wall mentions the intimate association with other mentally ill relatives, thereby stressing the element of contagion. He does not say whether there might not have been a hereditary element, but he is able to give evidence of the possibility of direct environmental influence. He has shown evidence of such influence in the type of father. In a significant number of cases, the school teacher daughter was the eldest child, the serious one, the one who was expected to shoulder responsibilities and who was prevented by circumstances from having the usual instinctive outlets.

There is perhaps some danger, in discussing a particular occupational or social group, that one will assume that persons in that group who suffer from the particular disease described are more numerous than is the case. It will be noted that Dr. Wall emphasized that teachers apparently do not have a high mental morbidity. Reports and statistics from various sources show marked differences with respect to incidence, type of disorder, age group and recoverability. It would be well if studies were made which would clarify these matters further.

Factors which are not easy to understand in these cases are the tendency to occultism and the hypochondriasis. Possibly the answer to the former is that the patients cling to the idea of omnipotence of the father and that they are conditioned or maintained in this belief by reason of their profession, which makes so much of the authoritarian ideology.

I have nothing of moment to add to the suggestions of treatment. In the case of patients outside a hospital, psychotherapeutic interviews need to be reasonably frequent and not too short, and vacation periods can sometimes be modified to be real vacations, rather than hectic interludes in which gain or study has been the main idea. Play and hobbies can thereby be acquired, and should prevent certain persons from becoming so ill that they need hospital care.

It might be well to mention the responsibilities which society has recently placed on the woman teacher. She is expected to overcome bad home situations, to foster patriotism, to blot out fascistic and communistic tendencies, to cure behavior problems and to prevent delinquency, to give sex instruction and, in addition, to get the child through examinations. That she occasionally becomes depressed and agitated can hardly be wondered at.

DR. LELAND E. HINSIE: Dr. Wall's communication is timely. It is as instructive as it is timely. For a long time people have discussed the personality of teachers without having appropriate facts at their disposal. Perhaps because the school teacher occupies such a unique position in society, perhaps also because children are turned over to her for training and experience and she takes over one's job as parent, one is prone to criticize her severely. It seems that there is one job in life for which every one is appropriately fitted, if one is to believe them —that is the job of being a parent. There are few, if any, parents who would dare to admit that they do not bring up their children better than any one else could. Consequently, any one who shares the responsibilities of parents must necessarily be the object of some unfavorable comments.

Dr. Wall's communication helps in a preliminary way to clarify the position of the teacher so far as she enters the field of psychiatry as a patient. He believes that school teachers do not constitute a large group of the total number of psychiatric patients. I myself share that opinion. During the past eight years, in a total of 2,700 patients admitted to the New York State Psychiaric Institute and Hospital, there were 19 school teachers.

It is interesting that among the 50 patiénts referred to by Dr. Wall, selected only on the basis of age, only three diagnostic groups were represented, namely, involution melancholia, dementia praecox and manic-depressive psychosis. The psychopathologic features had much in common and were built around the personal family life of the teachers. Moreover, it appeared that most of the teachers led relatively restricted lives.

It may help to dispel some fallacious notions about school teachers to know that of Dr. Wall's series one-half recovered and several were able to return to the school system in the capacity of teachers.

DR. EMIL ALTMAN: I am somewhat disappointed that the paper was limited mostly to patients in the fifth decade of life. Teachers do not begin to teach in the fifth decade. They begin to teach at the end of the second decade, and one finds that most of the psychoses develop before the end of the third decade. Furthermore, in my experience most of the cases are those not of manic-depressive psychosis but of dementia praecox.

A recent report by the Board of Regents of the State of New York shows that 12 per cent of the teaching force requires psychiatric treatment and that an additional 33 per cent is definitely maladjusted. I do not think that Dr. Wall wants to give the impression that only 2 per cent of the teaching personnel is psychotic. One must bear in mind that he limits his cases to patients in the fifth decade. At that age, even in New York city, half of the teachers are out of the system, so 2 per cent is not a fair estimate of the situation existing in greater New York.

It is a duty to build the next generation, and one hopes and expects that it will be an improvement on the present one. If this is to be accomplished, one must have better cooperation from the psychiatrist in private practice.

I want to ask for the cooperation of every private psychiatrist who examines a teacher. I do not think a psychiatrist helps a neurotic or a psychotic teacher by stating that "she is all right; she will be adjusted; all she needs is a little rest, and then she can go back to teaching."

Teaching is a hard profession, and good teachers are born, as good physicians are. In many ways the caliber of the teacher is of even greater importance than that of the medical man. If a patient who needs it is not treated or is treated improperly, he alone is harmed. If an ill teacher is permitted to continue in the classroom, she not only destroys her own life but impairs thirty or forty young lives every six months. Multiply this by the number of ill teachers and one obtains a sizable number.

I do not think it is fair for any trained psychiatrist to conclude that a teacher can be kept in a psychiatric hospital for six months or a year and then turned loose again to teach children.

I ask the cooperation of private psychiatrists, as of those in institutions. The psychiatrists in the New York state hospitals have been of great help, and I wish to take this opportunity to express my thanks to the superintendents of the various state hospitals and their co-workers.

I have with me Superintendent Greenberg, who is in charge of the teaching personnel. Dr. Greenberg is a layman, but I think even psychiatrists will find his experience and point of view illuminating.

DR. JACOB GREENBERG (by invitation): I am somewhat confused by the contradictory opinions of the experts. Dr. Altman, after examining a teacher whose mental condition is under suspicion, usually writes: "This teacher is not now and never will be in condition to render continuous and efficient service." And then the teacher's psychiatrist informs me: "While the teacher is ill the prognosis for recovery is excellent." I am glad to learn from Dr. Wall that many mentally ill teachers recover and are able to do their work satisfactorily. I wish to say that the Board of Retirement and the Board of Superintendents do all that is humanly possible to rid the schools of the mentally incompetent teacher. But it seems impossible to please Dr. Altman.

I am deeply interested in Dr. Wall's paper and in Dr. McGraw's remarks. I am glad to learn from Dr. McGraw that external "pressures" have a great deal to do with the incidence of mental disease among teachers. Dr. McGraw enumerates all the things which a teacher is expected to do in the course of a school day. Formerly, the teacher was expected to teach school—to teach arithmetic, history and geography—but today she is required to be father, mother and pastor. The demands made on the teacher are entirely too numerous. When Dr. Wall's statements and those of Dr. McGraw are available I shall place them in the hands of the Board of Superintendents.

May I sound a word of warning! While it is true that there are some ill teachers in the public schools, it is unfortunate that this information is given wide publicity. Such publicity accomplishes no good for the mentally incompetent

teacher and does great harm to the mentally competent one. The Board of Retirement, the Board of Superintendents and the Board of Education are cooperating in an entirely satisfactory manner with a view to retiring the mentally incompetent. These bodies must proceed in accordance with law. The rights of teachers must be protected. Dr. Altman cannot and should not be the "sole arbiter" on the professional life and security of the teacher.

DR. CLARENCE O. CHENEY, White Plains, N. Y.: I may state for Dr. Wall that the paper will be placed in the hands of any one who wishes to have it. This paper was presented to show the facts and with the thought that it might dispossess the minds of some persons of the idea that school teachers never recover from mental disease and are never fit to go back to school. I know some of the difficulties which the Board of Education has with teachers. I had some contact, twenty-five years ago, with a teacher who still is in school and who is still mentally ill, but who through legislative action maintained her position. That is an example of one of the difficulties of which I know. I know the difficulty also when a physician is faced with the question of maintaining his confidential relationship with a patient and at the same time of presenting the facts to the Board of Education. In so doing, he apparently causes a breach of that confidential relationship. The school teacher is still a patient of the physician, and she, like any one else, is entitled to the same degree of confidential relationship with her physician. It is a question whether the physician, without the patient's authorization, has any right to tell the Board of Education about the condition of that patient. I may say that at the Westchester Division of the New York Hospital we try to maintain the confidential relationship with the patient, and that no information is given about any patient, teachers included, without the authorization of the patient or a relative. At the same time, we never attempt to hide or cover up anything; we never give information that the patient is well and able to go back to school if we do not think she is able to do so. We have recognized for some time the difficulties of psychiatric examination which the Board of Education faces. If it had its own competent psychiatric examiners to whom to refer these teachers when they first become ill, it would not have to depend on outside physicians, with the possibility of breach of contract. I think that such a provision is a step in advance that might be made, should be made and cannot be made too early. There is need for a competent group of psychiatrists connected with the Board of Education to pass on the illnesses of teachers—psychiatrists who will understand that in some instances teachers will never get well and be able to go back to school and that others may have an illness such as any one may have, from which he will recover, may be competent to return to school and may be better than before and thus may be able to do better work, because of having had a nervous breakdown. Every case must be considered on its merits, in fairness to the children, to the Board of Education and to the teacher.

DR. JAMES W. WALL: I wish to thank those who have discussed the paper and to say that the group of teachers who become sick in the earlier decades have not come under my observation in great number.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

GILBERT HORRAX, M.D., *Presiding*

Regular Meeting, Feb. 16, 1939

ELECTRICAL BRAIN WAVES AND EMOTION IN MAN. DRS. HUDSON HOAGLAND, D. EWEN CAMERON and MORTON A. RUBIN, Worcester, Mass.

Electroencephalograms were recorded from 23 psychotic patients and normal persons who at intervals were stimulated emotionally by comments or questions known from the person's history to have produced emotional responses. Indif-

ferent material was also presented as a control. In a series of fifteen experiments on 12 subjects, pulse frequencies were measured with an electrocardiograph.

Both the frequency of the heart beat and the delta index (550 values) of the electroencephalogram were increased immediately after strong emotional stimulation in psychotic patients and in normal persons. The heart rate was also accelerated by a variety of indifferent stimuli when the subject was called on to play other than a passive, silent role in the experiment. This did not apply to the delta index, which thus appears to parallel more closely the presumed subjective emotion as judged from previous behavior of the subject during psychiatric interviews and from subsequent verbal admissions. The changes in the delta index were obtainable from various cortical areas (five experiments with 5 persons). Frequent repetition of the same emotional stimulus resulted regularly in adaptation of the delta index and, in the majority of cases, of the heart rate (six experiments with 6 persons).

It is concluded that the delta index is a measure of certain aspects of emotion. Further, in view of the fact that the delta index and the pulse rate show differential responses to emotional stimulation, the former gives indication of proving a valuable supplementary tool for the investigation of emotional reactions.

In a further study, electrical brain waves were recorded simultaneously with independent balanced amplifiers from the occipital cortex and from a lead (the H lead) placed far back in the roof of the pharynx near the hypothalamus, after a method described by Grinker. Five schizophrenic patients and 1 normal subject were used. At the H lead occurred alpha waves of a frequency similar to those occurring at the cortical lead. The percentage of time during which the alpha waves were present at the H lead was also roughly similar to that at the cortical lead from one person to another. The alpha waves at the two leads were not synchronous, although occasional bursts of alpha activity appeared roughly at the same time at the two leads. In a study on 14 dogs, Hoagland, Himwich, Campbell, Fazekas and Hadidian (*J. Neurophysiol.* **2**:276, 1939) have shown that a fine lead directly placed aseptically in the anterior portion of the hypothalamus gives electrical activity in the unanesthetized dog of the same type as that obtained by the Grinker technic. These investigators recorded simultaneously from the cortex and from the hypothalamus. The types and the relations of waves at the two leads in resting dogs were the same as those described here for man.

There is evidence that delta waves from the two leads occur together. When a patient was emotionally stimulated (probed) by being reminded of a matter known from his previous record to have been disturbing, there was usually a marked increase in delta wave activity at both leads for a minute or so following the probe. The pairs of delta waves were roughly synchronized, but control experiments indicated the essential freedom from conduction artefacts of the two recording systems. Eight experiments, involving about forty probings, were carried out on 4 schizophrenic patients, and the long wave activity at the two leads was quantified and plotted in terms of the delta indexes. The delta waves at the H lead preceded the corresponding delta waves at the cortical lead by an average of about four milliseconds. It is suggested that the delta waves from near the hypothalamus following emotional stimulation correspond to activity in this autonomic motor center, and that the corresponding cortical delta waves occurring a few milliseconds later may be the cortical signal of a conscious correlate of the emotional response.

The work discussed here has been published in full in two papers (Hoagland, H.; Cameron, D. E., and Rubin, M. A.: *J. Gen. Psychol.* **19**:227, 1938. Hoagland, H.; Cameron, D. E.; Rubin, M. A., and Tegelberg, J. J.: *ibid.* **19**:247, 1938).

DISCUSSION

DR. D. E. LINDSLEY, Providence, R. I.: The records from the hypothalamus look similar to those from the occipital cortex. It seems that they should be much more similar to the records from the motor cortex.

DR. HUDSON HOAGLAND, Worcester, Mass.: I have no a priori opinion about this. Records I have taken in collaboration with Himwich, Campbell, Fazekas and Hadidian show that the anterior portion of the hypothalamus in the dog shows activity similar to that of the occipital cortex. The posterior portion (mamillary bodies) usually gives records with more fast wave components. These electrograms were recorded from unanesthetized animals after recovery from operations in which the leads were planted aseptically. The correspondence between activity from the cortex and the anterior part of the hypothalamus in dogs with activity from the same regions in man as shown by the Grinker technic is indeed striking.

DR. D. B. LINDSLEY, Providence, R. I.: Is there any possibility of securing a check-up from the optic tracts?

DR. HUDSON HOAGLAND, Worcester, Mass.: We found that direct records from the optic chiasm in dogs differ from the hypothalamic records.

DR. D. B. LINDSLEY, Providence, R. I.: What discomfort or danger accompanies the insertion of the hypothalamic lead via the nares in man?

DR. HUDSON HOAGLAND, Worcester, Mass.: By using a local anesthetic prior to the insertion the discomfort is small. No complications from infection have arisen.

DR. R. S. SCHWAB: Do the alpha waves from the hypothalamic lead fade out when the eyes are opened in the light?

DR. HUDSON HOAGLAND, Worcester, Mass.: We found that they did, and we have published two figures indicating the fade-out. There appears to be a longer latency, however, than one sees simultaneously from the occipital lead. Also the fade-out is not as clearcut. Grinker, on the other hand, has reported that the hypothalamic waves do not disappear with illumination. I presume this discrepancy is due to individual differences in subjects.

FACTORS INVOLVED IN STABILITY OF THE THERAPEUTIC EFFECT OF METRAZOL IN TREATMENT OF SCHIZOPHRENIA: REPORT OF ONE HUNDRED AND FORTY-SIX CASES. DR. LOUIS H. COHEN, Worcester, Mass.

Data are presented on the therapeutic outcome in a group of 146 schizophrenic patients six months after cessation of daily treatment with metrazol. As others have pointed out, therapeutic results are better in younger patients, with a short stay in the hospital, and in those whose illness has been of short duration. Diagnostic differences in subtypes or differences based on sex cannot be demonstrated. It is found that the stability of therapeutic effect as compared one month with that six months after cessation of treatment depends on whether full remission has occurred. Of patients who achieved full remission, 89 per cent remained well after six months. On the other hand, of patients who had shown much or slight improvement after one month, 70 per cent had had a relapse after six months. The rate of remission for patients who had been ill for less than one year was 59 per cent. The conclusion is drawn that anything less than a full remission with this therapy must be considered with pessimism, as regards the ultimate clinical status, although, in about one third of the cases, amelioration of the patient's institutional adjustment may be expected to persist.

THERAPEUTIC SIGNIFICANCE OF FEAR IN THE METRAZOL TREATMENT OF SCHIZOPHRENIA. DR. LOUIS H. COHEN, Worcester, Mass.

A method is described in which a physiologic state similar to, if not identical with, fear was induced. It was used in a series of 20 cases to investigate and compare the relative therapeutic significance of "fear" with that of the usual convulsive procedure in the metrazol treatment of schizophrenia. The method consists essentially of the slow intravenous injection of minimal amounts of metrazol. The "fear states" induced in this manner have a duration of from

a few minutes to several hours. The incidence of convulsive seizures can in this manner be fairly well controlled. In a group of 20 schizophrenic patients on whom this procedure was carried out on ten successive days the therapeutic outcome after one month was compared with that in the same group treated with ten daily convulsive seizures. The "fear of treatment" characterizing some patients was also studied in both procedures. It was shown that the procedure with "induced fear" was of less therapeutic value than that characterized by convulsions. Furthermore, the "fear of treatment," which was differentiated from "induced fear," was again shown to be of little or no therapeutic significance.

DISCUSSION ON PAPERS BY DR. COHEN

DR. ALEXANDRA ADLER: Did Dr. Cohen observe any parallelism between the degree of remission and the degree of amnesia? I ask this because one sometimes observes that patients have a retrograde amnesia which "bleaches out" essential features in the psychotic system. This is the result of organic processes within the brain caused by the treatment. It is conceivable that this may change the picture of the psychosis. Perhaps the production of such amnesia is the essential factor that brings about the change in the course of the disease.

DR. LOUIS COHEN, Worcester, Mass.: I cannot answer Dr. Adler's question directly. The point is an interesting one. Patients frequently show amnesia of greater or less severity for a longer or shorter period after treatment. My belief is that these amnesic states, sometimes associated with confusion, are often frightening to the patient. However, the amnesia seems invariably to disappear completely, and the patient may have a remission regardless of whether or not amnesic states have characterized the treatment.

DR. J. M. THOMAS, Wellesley, Mass.: Does Dr. Cohen wish to leave the impression that the proportion of total successes resulting from metrazol treatment is only 14 per cent?

DR. LOUIS COHEN, Worcester, Mass.: For the 146 unselected patients studied the rate of remission is 14 per cent. I think, however, that the case material is "negatively" loaded. This rate is fairly good for a group so unselected. Malzberg's recent study does not give information on the rate of spontaneous remission for patients ill for less than one year.

DR. J. M. THOMAS, Wellesley, Mass.: Some hospitals report a higher rate than that.

DR. LOUIS COHEN, Worcester, Mass.: Nevertheless I wonder whether the rate of spontaneous remission is as high as 59 per cent for patients who have been ill less than one year? If one receives the patients early, most of them will "recover" and, apparently, stay well. The pessimistic note here is due to the fact that my patients were unselected.

DR. GILBERT HORRAX: Are there data on the rate of spontaneous remission at the Worcester State Hospital or at any state hospital?

DR. LOUIS COHEN, Worcester, Mass.: My colleagues are now collecting such data concerning about 5,000 schizophrenic patients. The published data are conflicting.

DR. JOHN ROMANO: Recently, my colleagues and I conducted a prognostic study of 600 schizophrenic patients who had been admitted to the Colorado Psychopathic Hospital, Denver, in the period between Jan. 1, 1933 and Dec. 31, 1936. We examined personally 345 of the 600 patients. Of the 345 patients, 247 were in hospital for mental disease. The remaining 98 were employed or at home. Only 1 patient satisfied all the rigid criteria for full remission. However, 80, or about 23 per cent, of the 345 patients were considered improved. It is our opinion that previous prognostic studies on schizophrenia have been of little value. Two notable exceptions have been the studies of Manz, in Marburg, Germany, and Langfeldt, in Oslo, Norway. The most outstanding difficulty in the studies of prognosis has been the great variation in conceptual views of the disorder. This disparity is not only international but national,

and even local. Some studies have included too few patients for statistical validity. Most have depended on social investigation and questionnaire methods. We were able to demonstrate an error of 50 per cent in comparing data obtained by questionnaires with those derived from actual examinations. There should be a sufficient interval, so that statistics on the course of the disease should not be confused with statistics concerned with episodes. Last, there should be some agreement as to the criteria for the final forms. Certainly, the concept of social remission is a broad one and may include all degrees of arrest and improvement. More confusion exists when one compares the various criteria for full remission.

DR. ISADOR CORIAT: Dr. Cohen's paper and most of the material on the psychologic aspects of metrazol treatment raise the question of what constitutes schizophrenia. This question is important, because the term has been given such a wide connotation by Bleuler. As to the criteria for recovery, I agree with Dr. Romano. The fact that a patient has made a social recovery does not mean that he has made a psychologic recovery, for some patients apparently make a 100 per cent social recovery and yet there are residuals of the original schizophrenic process.

I have always been puzzled by the question which Dr. Cohen raised: whether fear is a therapeutic agent in recovery. From a psychologic standpoint I cannot conceive of this. Fear in the case of a schizophrenic patient is certainly far more terrifying than in that of a patient with an ordinary psychoneurosis, such as anxiety hysteria, yet fear has not the slightest therapeutic effect on the outcome of psychoneurotic disorders.

DR. LOUIS COHEN, Worcester, Mass.: The question of fear in relation to the therapeutic efficacy of a treatment is often raised. I wish to say that the argument should concern not the question of fear as such, but whether there is something about the fear in the specific treatment that makes the patient prefer to get well rather than to submit to the treatment.

METRAZOL TREATMENT IN CASES OF DEPRESSION. DRS. FRANCES COTTINGTON and ARTHUR J. GAVIGAN, Worcester, Mass.

Metrazol therapy was carried out on a group of 20 depressed women patients with illnesses classified as manic-depressive and involutional psychoses. The ages of the patients ranged from 28 to 59, and the illness had lasted for from two months to five years. Treatments were administered three times a week, with an initial dose of 3 cc. of a 10 per cent aqueous solution of the drug, which was increased as necessary to cause grand mal seizures; the treatment was discontinued when remission or considerable improvement had taken place. Seventeen patients experienced full remission of symptoms, and 3 manifested improvement. These results indicate that further trial of metrazol in the treatment of depressions is warranted.

DISCUSSION

DR. ARTHUR J. GAVIGAN, Worcester, Mass.: During this work on the metrazol treatment of the melancholias we were interested in the phenomena occurring during treatment and the mechanism responsible for recovery. There seemed to be two possible mechanisms responsible for the changes observed. One was the production by metrazol of a psychologic change which enabled the patient to repress material of causal significance. Another possibility was a physiologic change which produced lifting of the depressed mood and with this ability to repress the material. Since it appeared that the mood lifted before the disappearance of the delusional ideas, the latter possibility seems the more probable. It was also observed that after recovery the patient showed no anxiety when material which had been expressed during the psychosis was discussed. In fact, the patient considered it amusing. However, the patient showed anxiety when certain events of the past life were discussed. The anxiety was of short duration.

DR. C. P. FITZPATRICK, Providence, R. I.: Of a series of 17 patients treated by Dr. B. T. Bennett at the Butler Hospital, 8 complained of pain in the back.

Roentgenograms were taken because cases had been reported in which the transverse processes of the spine had been fractured during metrazol convulsions. In all 8 cases of pain in the back there were compression fractures, of varying degrees. I shall refer to 2 cases in particular. In 1, the patient, after the first convulsion, complained of slight pain. After the third convulsion the patient complained of very severe pain. The roentgenogram showed fracture of the body of the eleventh dorsal vertebra, with buckling of the anterior inferior margin. There was more extensive compression of the body of the twelfth dorsal vertebra. Lateral views revealed slight, but distinct, kyphosis. There was no other evidence of vertebral injury. The second patient, a woman aged 30, had fifteen convulsions; after one or two she occasionally mentioned pain in the back and continued to do so during the course of treatment. The pain became more marked as treatment progressed. Roentgenograms revealed slight compression of the fourth and fifth dorsal vertebrae. The compression of the body of the sixth dorsal vertebra was of greater degree, with narrowing of the anterior margin and irregularity of the superior margin. There were a slight degree of kyphosis and a moderate amount of S-shaped scoliosis.

In the 8 cases the fractures were most frequent in the middorsal region.

In a small series of cases of involutional melancholia treatment with metrazol resulted as favorably as Dr. Cottington has reported.

DR. LOUIS COHEN, Worcester, Mass.: What technic was used in administering the metrazol?

DR. C. P. FITZPATRICK, Providence, R. I.: Metrazol was injected with the patient lying on his back. After the injection the physician, at the proper time, inserted a mouth gag and supported the jaw, while three nurses restrained the patient's arms and legs manually to prevent too great amplitude of movement and possible fractures or dislocations of the extremities. The nurses were instructed not to hold the arms or legs too rigidly but to yield with the patient's movements. This technic has been checked by an orthopedic surgeon and a roentgenologist.

DR. LOUIS COHEN, Worcester, Mass.: That seems to be more restraint than my associates and I have used. We have not had compression fractures, but we have taken relatively few roentgenograms. Four patients had fractures of the transverse process, which seemed to have been due to improper holding. For example, it was learned that an attendant had thrown himself across the patient and in that way, apparently, had caused the fracture.

DR. C. P. FITZPATRICK, Providence, R. I.: That was not the cause of the fractures in my cases.

DR. LOUIS COHEN, Worcester, Mass.: The fractures in my cases seemed to have been produced in that way. However, Dr. Fitzpatrick describes compression fractures, and I do not know how they could have been produced, except by overflexion of the vertebral column.

DR. C. P. FITZPATRICK, Providence, R. I.: Compression fractures of the vertebrae are produced by acute anterior flexion of the vertebral column. It has been observed, since the fractures were discovered, that just previous to the tonic phase of the seizure some patients have sharp anterior flexion movements, from four to six in number and lasting a few seconds. It is the opinion of the orthopedic surgeon, the roentgenologist and my colleagues and myself that it is in this period that the fractures occur. The flexion movements are not present in every case, but some patients consistently show this motor pattern at the beginning of the seizure. With the assistance of the orthopedist a technic is being worked out which will help to control the amplitude of these initial flexion movements and thus reduce the possibilities of spinal fractures.

DR. J. M. THOMAS, Wellesley, Mass.: I have noticed marked changes in memory after a course of treatments with metrazol. Are not patients in the involutional period a dangerous group in whom to produce convulsions?

DR. FRANCES COTTINGTON, Worcester, Mass.: Loss of memory was complained of, but when the patients were pinned down and questioned we thought that it was due rather to lack of concentration. This symptom always disappeared before the patient left the hospital.

DR. J. M. THOMAS, Wellesley, Mass.: I did not have such fortunate results.

DR. EMERICK FRIEDMAN, Waltham, Mass.: I purposely delayed discussing these papers until both had been read. With regard to the first paper on metrazol, I wish to ask what is known about fear. Papers have been written about fear as a therapeutic agent, and it is not possible to disregard this factor entirely. Fear is not classifiable. In the first place, fear in the sense in which a psychotic patient has fear is not the same as fear that a patient feels during treatment. Fear during treatment is almost entirely somatic; the patient soon changes his fear reaction from a psychologic response to a feeling of personal dismemberment, whether symbolic or factual. After the patient has felt this "disintegration," he may, analytically speaking, reconstruct his ego—death and rebirth.

The question of comparing the rate of therapeutically induced remissions with that of spontaneous remissions is difficult. When neurosurgery had not yet reached its present state of development, neurosurgeons treated tumors of the brain with iodides and preferred to delay making a diagnosis until the death of the patient. It was similar in cases of schizophrenia. When one made a diagnosis of schizophrenia the story was regarded as ended. One had to tell relatives that the patient had schizophrenia, or dementia praecox. "Some may recover, but the chances are rather slim." Since attempts have been made to treat patients with metrazol and insulin there seems to be a more hopeful outlook for schizophrenia. It is said that schizophrenia may not have been hopeless. Perhaps the most that is being accomplished is to stimulate the patient, but interest has been created in direct attacks on the schizophrenic organism by means of potent drugs.

I wish to ask Dr. Cohen whether his routine of treatment was designed for therapeutic or for experimental reasons.

DR. LOUIS COHEN, Worcester, Mass.: This was a therapeutic procedure studied in an experimental manner.

DR. EMERICK FRIEDMAN, Waltham, Mass.: In a recent paper, von Meduna and I expressed our opinion as to the role of fear in the convulsive treatment and as to the question of fractures complicating treatment with metrazol and camphor (The Convulsive-Irritative Therapy of the Psychoses, *J. A. M. A.* **112**:501 [Feb. 11] 1939). It was shown that patients so treated usually are not, and have not been, active muscularly for some time before treatment is begun. Therapy is instituted that causes severe strain on the whole skeletal system, which is not prepared for this work from the vitamin standpoint because of previous dietary insufficiencies.

PHILADELPHIA NEUROLOGICAL SOCIETY

JOSEPH C. YASKIN, M.D., *President, in the Chair*

Regular Meeting, Feb. 24, 1939

BIOLOGIC EXPERIMENTAL CATATONIA: HUMAN AND BULBOCAPNINE CATATONIA AND EXPERIMENTAL CATATONIA FOLLOWING DISTURBANCE OF HEPATIC FUNCTION. DR. HERMAN DE JONG, Amsterdam, Netherlands (by invitation).

Experimental catatonia (de Jong, H., and Baruk, H.: La catatonie expérimentale par la bulbocapnine, Paris, Masson & Cie, 1931), as my colleagues (Baruk and others) and I understand it, consists of the following phenomena, which may be considered as analogous to the syndrome of human catatonia: A. After

administration of a small dose: (1) catalepsy—active retention of postures given to animals or man; (2) negativism—passive or active resistance to change of attitudes already assumed; (3) autonomic phenomena—e. g., polypnea and salivation. B. After administration of a large dose: (1) hyperkinesia and abnormal postures.

Later, my collaborators and I observed that the catatonic syndrome can be produced in different ways—by administration of a great number of chemical substances, by electric currents, by surgical interventions on the brain and, last but not least, by experimental autointoxication. Finally, we formulated the idea of experimental catatonia as a frequently occurring reaction of the central nervous system.

Among the large number of substances able to produce the phenomena mentioned are many known to occur in human metabolism. 1. Experimental Hormonal Catatonia. We were able to produce catatonic phenomena in cats and mice by injection of acetylcholine and by a large dose of epinephrine. 2. Catatonia by Asphyxia. We proved that catatonic phenomena may arise during certain conditions of asphyxia. Among the substances which can produce such asphyxia may be mentioned such biologic substances as nitrogen and carbon dioxide. When a mouse that has been kept for some time in a glass containing carbon dioxide is replaced in ordinary air, the phenomena shown by the animal resemble those produced by injection of toxic substances, but they occur in reversed order. Here one can study the phenomena shown by the animal recovering from a maximal dose of the toxin. 3. Autointoxication. The theory of self intoxication as a cause of human catatonia has often been mentioned by authors, such as Kraepelin, Jelgersma and Serieux.

With the assistance of Kok, Geesink and Nieuwenhuyzen and den Hartog Jager I studied this subject experimentally. Our aim was to produce lesions in certain organs (spleen, kidneys, testes, liver and intestine). We expected that experimental catatonia could be produced under these conditions, since in this way substances are introduced into the circulation which may have a toxic effect on the central nervous system.

We found that experimental catatonia in dogs does not appear after extirpation of the spleen, kidneys or testes or combinations of these organs. Injections of extracts of these organs into mice did not produce catatonic phenomena.

Catatonia Produced by Intestinal Obstruction: However, we were able to produce experimental catatonia by obstruction of the intestine in 4 of 12 experimental dogs. Artificial ileus, with obstruction at two places, gave these results.

Catatonia Produced by Hepatic Insufficiency: We performed experiments on a larger scale concerned with elimination of hepatic function in animals. We were especially interested in the part played by the liver, as the problem of hepatogenic insufficiency has often been mentioned in psychiatric literature, for instance, by Lingjaerde. We succeeded in producing distinct catatonia after ligation of the hepatic artery in the cat. In experiments in collaboration with Geesink and Nieuwenhuyzen, the hepatic artery of 36 cats was ligated. Twelve animals died immediately after the operation. Of the other 24 cats, 16 showed phenomena of experimental catatonia, viz., negativism and catalepsy. The catatonia was often distinct, and sometimes as intense as that produced by bulbocapnine.

Another method of partially eliminating the filtrating function of the liver consists of making an anastomosis between the vena cava and the vena porta (Eck's fistula). Dr. Geesink successfully performed this difficult operation in 4 dogs. One of the dogs showed no neurotoxic symptoms whatever. The animal remained alive and grew thin, but motility, reflexes and other neural functions remained normal. Another dog showed symptoms of blindness, with normal motility. The 2 remaining dogs showed such neurotoxic symptoms as can be classified only as experimental catatonia. One of these 2 dogs showed these symptoms distinctly for about ten days; thereafter, motility again became normal. The second dog exhibited spontaneous catatonia, off and on, for about one month.

During this period its susceptibility to bulbocapnine catatonia was enormously increased. The catalepsy was manifested by the animal's maintaining its front legs in a crossed position, which a normal dog never does. The negativism was exhibited by the animal's objecting more strenuously to a change of attitude than under normal circumstances. After a month the catatonic symptoms disappeared, which may be explained by the fact that adhesions were formed between the liver, stomach and intestine, as shown by necropsy. This also explains why 1 of the dogs with Eck's fistula showed no neurotoxic symptoms.

I have tried to indicate briefly the large field which my collaborators and I have explored in our laboratory. The work was done after having formulated, with Baruk, the concept of the syndrome of experimental production of catatonia with bulbocapnine. After the Rockefeller Foundation enabled us to work on a larger scale, we demonstrated that experimental catatonia is a frequent, and not a specific reaction, of the central nervous system. Although experimental catatonia is not, in a narrow sense, specific, when one traces the ways of producing it by biologic methods, especially by autointoxication, one finds some specificity. Of the organs examined, we found that autointoxication from the intestines and liver alone can produce experimental catatonia.

DISCUSSION

DR. E. A. SPIEGEL: I congratulate Dr. de Jong particularly on the experiments having to do with toxins originating in the body itself. I wish to ask, in this connection, whether the central nervous system of the animals has been studied. About ten years ago, Huff reported having produced Eck's fistula in dogs; by that means alone he did not succeed in inducing the optokinetic symptoms. When he intoxicated the dogs they showed optokinetic symptoms. These experiments are comparable with those of Dr. de Jong.

DR. D. W. BRONK: While Dr. de Jong was reading his paper I wondered whether he would be willing to venture an opinion as to what happens in the cells of the central nervous system, and whether he has any idea what causes the persistence of a postural discharge, so to speak. I wish also to ask what is the effect of bulbocapnine or other products in the case of a spinal anmial, and what are the common factors in the various processes which produce experimental catatonia?

DR. A. ORNSTEEN: This demonstration is in conformity with theories being expounded in regard to certain types of rigidity in their positive phases and in the catatonic states produced by certain drugs. The use of benzedrine has been well established in the minds of some clinicians, but in my experience, which is limited, I have not found that it does much to relieve the rigidity. It assisted materially in treatment of mental torpidity, but I did not notice any relief from the catatonic types of rigidity. Will Dr. de Jong express an opinion as to where the effect of bulbocapnine lies.

DR. HERMAN DE JONG, Amsterdam, Netherlands: Studies on the brains of the dogs with catatonia of hepatic origin are of interest, but the preparations have only just been finished. Hence, I cannot answer this question at the moment.

The work of Dr. Spiegel seems to me of great importance for the understanding of the pathologic mechanism of the catatonic syndrome. As for antidotes, I do not agree with Dr. Spiegel. I have given carbon dioxide and other chemical substances to catatonic monkeys, but I have the impression that these substances acted in the same way as large doses of bulbocapnine, viz., by producing hyperkinetic phenomena. It occurred now and then that hypokinetic and hyperkinetic movements were in equilibrium. The animal then walked a little, and afterward convulsions or catalepsy reappeared. It was a matter, therefore, of superposition of hyperkinetic and hypokinetic phenomena and not of normal walking.

Dr. Bronk asked about the physiologic mechanism. I can merely hypothesize. What is needed is a man like Dr. Bronk to make experiments on cellular dis-

charge in experimental catatonia. There is the possibility that the common factor in all the different methods by which catatonia can be produced is a kind of cellular asphyxia. Thus, the threshold of discharge of motor cells is changed by intoxication with different drugs, and energy may radiate automatically, thus giving rise to chronic tetanic innervation in different groups of muscles, which forms the basis of catalepsy.

I thank Dr. Ornsteen also for his remarks. As to the localization of catalepsy: The motor cortex seems important. If one studies experimental catatonia in the animal series, one finds that animals without a neocortex, such as frogs, do not show catalepsy after administration of bulbocapnine. In birds the neocortex appears, and Dr. G. W. Henry, who collaborated with me, showed that catalepsy can be produced in them, but less distinctly than in mammals. Another group of experiments has been performed by making surgical lesions in different parts of the brain. In some cases spontaneous "surgical" experimental catatonia appeared, but the conclusions concerning localization of catatonic phenomena thus obtained were different from those for the animal series. The problem of localization, therefore, is still unsolved. It is even possible that catalepsy can be obtained from different levels of the central nervous system.

POSSIBLE ETIOLOGIC ROLE OF INORGANIC ARSENIC IN DISTURBANCES OF THE CENTRAL NERVOUS SYSTEM ATTRIBUTED TO AVITAMINOSIS, WITH SPECIAL REFERENCE TO PELLAGRA (PRELIMINARY REPORT). DRS. MICHAEL SCOTT and ERNEST E. AEGERTER.

This paper will be published in full in a future issue of the ARCHIVES.

FRIEDREICH'S ATAXIA ASSOCIATED WITH DIABETES MELLITUS. DRS. NATHAN S. SCHLEZINGER and KURT GOLDSTEIN, New York.

Although the introduction of insulin as a specific and effective mode of therapy of diabetes has resulted in a radically altered prognosis, the etiologic and pathologic features of this endocrine disorder have in many respects remained enigmatic. Therefore, when one finds linked two conditions such as Friedreich's ataxia and diabetes mellitus, a careful study of the individual cases is indicated, with the hope of discovering unknown factors which may lead to a better understanding of one or both of the conditions.

The following description constitutes a brief summary of the clinical records of two sisters who manifested diabetes mellitus during the course of a specific neurologic disorder, Friedreich's ataxia.

CASE 1.—A girl aged 13 years was first hospitalized on Aug. 28, 1930, with a history of unsteadiness in walking since 6 years of age. The neurologic picture was characteristic of Friedreich's ataxia and was associated with evidences of status dysraphicus and polyglandular endocrine dysfunction. There were a gradual progression of neurologic symptoms and the development of diabetes mellitus at the age of 15.

CASE 2.—A woman aged 22 was first hospitalized on June 18, 1932, with a history of difficulty in walking, which had appeared, with the menarche, at 15 years of age; diabetes mellitus developed at the age of 21. The neurologic picture was characteristic of Friedreich's ataxia and was associated with evidence of polyglandular endocrine dysfunction. There was gradual progression of neurologic symptoms.

The characteristic semeiology of Friedreich's ataxia is well demonstrated in both cases and needs no emphasis. Besides various extraneural anomalies, these patients showed evidence of endocrine dysfunction in the form of hypopituitarism, hypothyroidism and hypogonadism. In addition, a striking feature in both cases was the apparently specific, limited concurrence of diabetes mellitus with Friedreich's ataxia.

A review of the literature discloses that the concurrence of diabetes mellitus and Friedreich's ataxia has been reported previously in no less than 18 cases. Familial incidence has been noted four times, affecting a total of 9 patients, and without exception diabetes was present only in siblings affected by Friedreich's ataxia, while the reverse was not true. In all instances the onset of the neurologic disorder antedated the onset of diabetes, usually by many years.

Various pathogenic hypotheses for this disease combination are considered. Hereditary predisposition and neurogenic diabetes are thought to be the more likely factors. They are discussed as to their relative merits and their correlation with clinicopathologic and experimental data.

In view of the existence of generalized endocrine hypofunction, including hypopituitarism, it is believed that these cases serve as a warning against hasty acceptance of the pathogenic concept of diabetes mellitus which is based on the "diabetogenic" action of the hypophysis. These cases also serve to direct attention to portions of the central nervous system which regulate the functions of the autonomic nervous system and to indicate reexamination of the evidence which may support the hypothesis of a reciprocally interacting neuroendocrine mechanism.

Our investigation seems to indicate that the extent of involvement of the central nervous system in Friedreich's ataxia is considerably greater than is ordinarily supposed. Therefore, the importance of making complete neuropathologic examinations in this neurologic disorder is emphasized.

DISCUSSION

DR. J. C. YASKIN: One point that Dr. Schlezinger emphasized is that if there is an endocrine disturbance in Friedreich's ataxia it is a tendency to hypofunction. At the Philadelphia General Hospital a patient with typical Friedreich's ataxia had a sister in the women's department with a marked hyperthyroid condition. Unfortunately, I do not remember the values for sugar metabolism. The surgeon was unwilling to subject the patient to thyroidectomy. This was a case of marked hyperfunction of the thyroid gland, with no evidence of gross pituitary disturbances.

DR. G. D. GAMMON: The question of diabetes in relation to hypothalamic lesions might justifiably be introduced here, since it has been suggested that his disorder may be linked with a hypothalamic lesion. So far as I know, persistent diabetes has never been produced experimentally in animals, except in 1 case reported by a German investigator, who introduced silver nitrate. He thought that the lesion was an irritative rather than a destructive one.

Clinically, one sees diabetes, which may be sporadic, associated with lesions in the central nervous system, and the diabetes may be serious.

DR. B. J. ALPERS: I was unacquainted personally with the association of diabetes and Friedreich's ataxia until Dr. Schlezinger called it to my attention. These cases are interesting in view of his remark that he couldn't make any statement concerning certain features of this association because most of the examinations had been made on the spinal cord. I think this point illustrates well the myopia of neuropathologists who study one part of the nervous system, with complete neglect of others until attention is called to them. Another feature of interest is that there was no homochronicity in the present cases. In 1 case the diabetes appeared at the age of 15 and in the other at 21. Is homochronicity shown in other cases in the literature? Second, I was not entirely convinced of the actual relation between Friedreich's ataxia and diabetes mellitus. Is there any greater incidence of familial diabetes in cases of Friedreich's ataxia than there is in cases of diabetes in general? I wish to ask if neurogenic diabetes reacts to insulin.

DR. NATHAN S. SCHLEZINGER: In response to Dr. Yaskin: There has been an occasional report of hyperthyroidism in cases of Friedreich's ataxia. As to the incidence of thyroid dysfunction: In a review of the literature one finds a great deal of emphasis on the symptoms of hypofunction. It is known that hyperthyroidism may occur as a transitional feature in such cases.

I agree with Dr. Gammon that the diabetic conditions produced experimentally by neural lesions are usually transient. The only clinicopathologic study, I believe, is a report by Vonderahe showing pathologic changes in the hypothalamus.

In regard to the question of homochronicity raised by Dr. Alpers, I wish to state that, in abbreviating the presentation here, I omitted evidence significant in that respect. In the second case the onset of Friedreich's ataxia was at the time of puberty; in the first case, at the age of 6, after diphtheria. Therefore, there are two facts here which emphasize that precipitating factors may affect the time of onset of the neurologic disorder. As to the other cases in the literature, the theory of homochronicity held good in general. I think here one is dealing with other etiologic factors. The appearance of diabetes in the families of patients with Friedreich's ataxia seems to be definitely answered in the negative; that is, diabetes does not occur in other members of the family. In every case reported in these families in which diabetes developed there was also Friedreich's ataxia; however, the latter did exist alone, without the occurrence of diabetes. Therefore, I think it is beyond the possibility of coincidence to explain adequately the intimate association of diabetes with Friedreich's disease. In this connection it is also important to emphasize that the onset of Friedreich's ataxia always antedated that of diabetes.

INTERFERENCE PHENOMENA BETWEEN OPTOKINETIC AND LABYRINTHINE NYSTAGMUS. DRS. E. A. SPIEGEL and N. P. SCALA, Washington, D. C. (by invitation).

The subcortical type of optokinetic nystagmus was studied in cats before and after bilateral lesions in the vestibular nuclei. A variety of interference phenomena between the subcortical optokinetic nystagmus and central labyrinthine nystagmus was observed. The optokinetic impulses may increase "spontaneous" central labyrinthine nystagmus if synergic in direction; they may diminish and occasionally reverse it if antagonistic in direction. Large lesions of the vestibular nuclei may prevent the production of subcortical optokinetic nystagmus in one or both directions, even if the reticulate substance is not affected. The experiments suggest that the vestibular nuclei play an important part in transmitting to the nuclei of the ocular muscles the impulse from the superior colliculi innervating subcortical optokinetic nystagmus.

DISCUSSION

DR. J. C. YASKIN: My question is important from a clinical standpoint and may have some bearing on this problem. Can nystagmus occur from lesions limited to the cerebrum, that is, from lesions not of the posterior fossa? If so, does this nystagmus have any relationship to the type of nystagmus reported?

DR. A. ORNSTEEN: Since Dr. Spiegel is here, I wish to ask him how he would explain the appearance of optokinetic nystagmus in persons who have lesions high in the cervical region of the cord.

DR. E. A. SPIEGEL: Nystagmus in cortical disease, chiefly in cases of tumors, is usually a pressure phenomenon on the lower parts of the brain. In addition, one can produce nystagmoid movements by stimulating the frontal or occipital lobes; first, there occur tonic movements of the eyes; as the stimulus increases there are clonic eye jerks; if I were to make a graph of these spasms and show it to some one without saying what it was, he would say it represented nystagmus. In other words, one can produce clonic eye jerks by stimulation which clinically resemble nystagmus. They are like epilepsy of the ocular muscles. The explanation, I believe, is that the centrifugal pathways of the frontal and occipital oculogyric centers act on the vestibular nuclei. There is another possibility of the origin of the nystagmus in cortical disease. If a patient has cortical destruction on one side, this results in a disturbance of equilibrium between the labyrinths (*Nystagmusbereitschaft*). If there develops, in addition, slight labyrinthine stimulation, these peripheral, otherwise subthreshold, stimuli may be sufficient to produce nystagmus. One can see in cerebellar disease a similar phenomenon.

After destruction of the cerebellum overexcitability of the vestibular reflex arc may develop. The nystagmus in cases of lesions high in the cervical cord seems to be due to concomitant lesions of the vestibular nuclei. For instance, in cases of syringomyelia there is often at the same time formation of fissures in the fourth ventricle, reaching the vestibular nuclei.

PARALYSIS OF THE VOCAL CORDS: SUMMARY OF SEVENTY-FIVE CASES. DR. N. M. LEVIN.

Paralysis of the vocal cords may be the first sign of a serious lesion in the neck, chest or central nervous system. In this paper, only cases are considered in which the recurrent laryngeal nerve was involved, anywhere from its source in the trunk of the vagus nerve from a center in the medulla in the floor of the fourth ventricle to its final distribution to the intrinsic muscles of the larynx. Cases of lagging of the vocal cords as a result of tuberculous infiltration of the cords or the arytenoid cartilages or of inflammatory reaction in the laryngeal muscles are excluded in this presentation.

(Slides were shown reviewing the anatomic relations of the recurrent laryngeal nerve from its exit [in the vagus trunk] from the skull by way of the jugular foramen, its course through the thorax and its final distribution in the larynx.) The 75 cases, with the cause of paralysis, are listed in the following tabulation.

Cause of Paralysis	*Number of Cases*
Complications following thyroidectomy (bilateral)	14
Complications following thyroidectomy (unilateral)	9
Mediastinal growths	6
Aortic aneurysm	3
Lesions of the central nervous system	5
Lesions of the neck	5
Laryngeal lesions	4
Peripheral neuritis	1
Old pulmonary tuberculosis	4
Pleural thickening	3
Pneumonoconiosis	1
Pleural effusion	3
Pulmonary neoplasms	3
Heart disease	2
Carcinoma of the esophagus	2
Calcified hilar node	1
Complications following diverticulectomy	2
Multiple causes	1
Cause undetermined	4
Ankylosis of the cricoarytenoid joint of the larynx	2
Total	75

In reviewing this series one notes that in a third of the cases the condition was postoperative. In the remainder the causes were varied. One was led to believe by early writers that aortic aneurysm is a common cause. My study does not bear this out.

In lesions of the central nervous system, owing to the proximity of the ninth, tenth, eleventh and twelfth cranial nerves, associted paralysis results, in addition to the involvement of the vocal cords, so that a great variety of syndromes may result, such as those of Avellis and Burnett. Peripheral neuritis may cause transient paralysis. Ankylosis of the cricoarytenoid joint of the larynx must be recognized as a clinical entity in the causation of paralysis of the vocal cords (arthritis). Laryngoscopic examination is often necessary to make a final diagnosis.

(A series of slides were shown demonstrating many lesions of the central nervous system, credit being given to Dr. A. C. Furstenberg for his article [An Anatomical and Clinical Study of Central Lesions Producing Paralysis of the Larynx, *Ann. Otol., Rhin. & Laryng.* **46**:39, 1937], and lesions in the neck, thorax and mediastinum which were the cause of paralysis of the vocal cords. A moving picture in natural color showing normal vocal cords in a living patient and several showing unilateral and bilateral paralysis were presented.)

DISCUSSION

DR. A. ORNSTEEN: I notice that in one of the series of 75 cases the condition was referred to as peripheral neuritis. Was it localized neuritis or part of general peripheral neuritis following influenza? I am interested because of the occasional cases of isolated neuritis of the vagus nerve, with hoarseness and dysphagia; I should like to ask Dr. Levin whether in his experience at the Jackson Clinic he occasionally encounters a patient who has unexplained unilateral paralysis of the vocal cords which adjusts itself for no known reason. I have in mind the case of a woman who, after extraction of a tooth, had prostration for two days and headaches, and on the third day difficulty in swallowing. Her voice changed, and she had unilateral paralysis. After all other better known causes were excluded, the condition was found to be peripheral neuritis of the vagus nerve following extraction of a tooth, such as one more often sees affecting the facial nerve. I wish to know if that would be an acceptable diagnosis in the Jackson Clinic. The patient, in three months, recovered completely.

DR. MICHAEL SCOTT: This presentation illustrates the value of examination of the vocal cords. In a case of osteoma of the base of the skull presented here a few years ago (Scott, Michael: An Interesting Case for Diagnosis, ARCH. NEUROL. & PSYCHIAT. **36**:879 [Oct.] 1936) it was interesting that the boy could sing the scale well and that the paralysis of the vocal cords would have been missed entirely had not a laryngeal examination been performed.

DR. J. C. YASKIN: I am amazed that of the 75 cases there were only 5 or 6 in which the condition was definitely due to diseases of the nervous system. My impression is that involvement of the recurrent laryngeal nerve is much more common than the impression gained from these statistics. I can recall 1 or 2 cases of primary tumors and suppurations of the base of the skull; finally, I think there were some cases of involvement of the vocal cords associated with tumors of the brain stem, of which a number are to be reported. One might be left with the impression that involvement of the recurrent laryngeal nerve is not as common a disease as was formerly thought. Perhaps Dr. Levin can give an explanation in his closing remarks.

DR. N. M. LEVIN: In answer to the questions by Dr. Ornsteen about peripheral neuritis, it can definitely be said that peripheral neuritis will usually clear up. There are other local causes of paralysis of the vocal cords. There are neuritis and myositis. The neuritis may be focal, if one wishes to call it that, and may clear up spontaneously. That has occurred several times and is a tenable diagnosis.

As to Dr. Yaskin's question about the limited number of lesions of the central nervous system: This was a selected group, and the commoner causes were ruled out elsewhere. They were referred to because of the difficulty in making a diagnosis. Dr. Ernest Spiegel and I discussed a case, in which he performed autopsy, which proves that Semon-Rosenbach's law can be shelved definitely.

Book Reviews

Histopathologie des Neurons. By Karl Schaffer and Desiderius Miskolczy. Price, 20 marks. Leipzig: Johann Ambrosius Barth, 1938.

The aim of this book, dedicated to the memory of von Lenhossék, is to show that "the normal neuron is topographically identical with the pathologic neuron" and that it "reacts differently to endogenous and to exogenous factors." An introductory chapter discusses in general the relation of the neuron theory to neuropathology and defines briefly the endogenous and exogenous types of reaction of the neuron to various pathologic agencies. In the endogenous reaction the ectodermal elements are primarily affected; in the exogenous, the mesodermal, with consecutive involvement of the neurons.

The endogenous reaction is discussed in the first part (pages 43 to 212). Hereditary diseases fall into this class. They are frequently circumscribed, and are then characterized by the disturbance (1) of a well defined system; (2) of a distinct segment of the neural tube (e. g., rhombencephalon or telencephalon), and (3) of exclusively neuroectodermal elements. This has been called by Schaffer the *Faktorentrias* (factorial triad). In contrast to the circumscribed forms, a generalized neuroectodermal electivity is exemplified by infantile amaurotic idiocy. As circumscribed hereditary diseases showing a factorial triad, hereditary spastic spinal paralysis, manifesting itself either as bulbospinal nuclear muscular atrophy or as amyotrophic lateral sclerosis, cerebellar ataxia and Huntington's chorea, are described by Schaffer in detail.

The intracortical systemic diseases are then considered by Miskolczy. Schizophrenia is discussed first. "Only those cases can be included in which the development of the characteristic symptoms is due to endogenous and idiopathic factors. Schizophrenic reactions of schizoid personalities have to be dismissed a priori as paratypical." Does that mean that the schizoid character is not due to "endogenous and idiopathic" factors? Surely, the heredity could be proved in many cases. According to Miskolczy, in schizophrenia nerve cells of the cortex disappear by a necrobiotic process, and in chronic forms the cortex shows islands of rarefaction, often indicated by an oblique position of the surrounding pyramidal cells. The third and fifth layers are most severely affected; layers VI, II and IV follow, in this order. The various cortical areas are not uniformly affected; the extension of the schizophrenic process is illustrated in two figures. "The schizophrenic process destroys the most human parts of the brain," the frontal, inferior parietal and temporal lobes. To judge by figure 45, the three convolutions of the frontal lobe appear to show differences in the severity of destruction.

Pick's disease and senile and Alzheimer's dementia are discussed as further examples of hereditary disease. Pick's disease affects the polar regions of the frontal and temporal lobes by preference. "These neencephalic regions, acquired by progressive cerebration, are the first to be victimized by Pick's disease." While the term "neencephalic" is used here in a sense different from that given it by most authors, Miskolczy's discussion, on the whole, is based squarely on modern cytoarchitectural achievements, in particular, on von Economo's great work. In figure 55, however, the letter "a" marks the supramarginal, and not the angular, gyrus, as stated in the text.

As an example of a generalized neuroectodermal disease, hereditary amaurotic idiocy is discussed by Schaffer, with a detailed description of the finer cellular changes. The differences between the Tay-Sachs and the Niemann-Pick form are stressed. The former is considered a purely ectodermal disease; the latter is characterized by a disturbance in the lipoid metabolism of the whole body, e. g., by changes in the mesodermal reticuloendothelial apparatus.

The second part (pages 213 to 396), concerned with the exogenous reactions of the neuron, deals in a first paragraph briefly with exogenous neurotropic diseases, such as poliomyelitis, lyssa and cholesterosis. In a second, much longer, paragraph on exogenous traumatic reactions, first wallerian, then transneuronal, degeneration and finally regeneration are treated. The wallerian degeneration of many important tracts in the spinal cord and the brain is described and illustrated. As an anatomist, the reviewer would have preferred further details about doubtful points to a review of pathways frequently described in the literature. The tracts from the sensory nuclei of the trigeminus nerve, for example, are described in one sentence, without the help of figures. The direct corticocerebellar tract, the cerebellar share (*Anteil*) of the pyramids, is mentioned, but no new observations are added to Schaffer's previous description. For the optic tracts and radiations, Minkowski's work is mainly relied on; the numerous recent contributions of English and American authors are not even mentioned.

Transneuronal degeneration is treated by Miskolczy. Crossed cerebellar atrophy, changes in the optic centers after unilateral peripheral blindness and other phenomena are cited as examples. Miskolczy differentiates degeneration of the neuron primarily affected, transneuronal degeneration of the first or second order and retrograde atrophy.

The chapter on regeneration contains several good photomicrographs, which appear to be new.

There is a list of references covering about 14 pages, in the abbreviated, space-saving way that is an irritating feature of modern German publications. Those that were checked proved to be correct. There is no alphabetic index.

The book contains interesting observations and a useful list of references. As a systematic exposition of the neuron theory it hardly attains the level of standard textbooks or handbooks.

Practical Child Psychotherapy. By Curt Boenheim. Price, 10s. 6d. Pp. 177, London: John Bale Medical Publications, Ltd., 1938.

"This book is based on the experience of the author gained when practicing in Berlin over a period of ten years as a child psychotherapist." The title of the volume is an index to its shortcomings as well as its virtues. It creates too much the impression of the possibility of rule-of-thumb treatment, which impression is reenforced by the writer's too great optimism in prognosis. Despite his frequent references to "depth psychology" (with which term he seems to relegate dynamic psychiatry to some esoteric limbo) and the necessity of its use "in certain cases," his approach to the problems of child psychiatry is essentially descriptive and deals with such general concepts as "precocious child," "overexcitable child," "nervous atmosphere," "inappropriate behavior of the father" and "unsatisfactory environment." The therapy is "practical" in the way that child guidance as practiced classically in the United States is practical. The general health is attended to; the environment is "altered"; the anxiety of the parents is allayed, and similar procedures are followed.

"The cases dealt with belong largely, although not exclusively, to the domain of the organic neuroses, although some chapters go far beyond this range . . . Careful selection has been made of those conditions which are most important from the point of view of the general practitioner and the children's doctor." In this connection the author refers to his methods of treatment as " 'minor psychotherapy' just as we speak of minor in contradistinction to major surgery." Unfortunately, the book does not make clear in a specific way the possible ramifications of the symptoms under consideration, so that the indications for "major psychotherapy" may be recognized.

Consideration is given to the alimentary disorders; urinary disturbances; disorders of sexual development, with special emphasis on masturbation; nervous habits; motor disorders, including tics, chorea, epilepsy and stammering, and a heterogeneous group, including "cardiac neurosis," vasomotor disturbances, migraine, asthma, acute and chronic illness and mental deficiency. There are an

extensive bibliography, referring largely to the German literature, and an appendix, in which is presented a schema for ascertaining the "mental-psychical" development of the child.

Personality in Formation and Action. By William Healy, M.D. Price, $2. Pp. 204. New York: W. W. Norton & Company, Inc., 1938.

This book can be easily comprehended by the intelligent layman, but it is by no means "popular." The author surveys the multiple factors affecting developing of personality and stresses the necessity of the intensive case study method for a valid analysis of these factors. He seems remarkably unbiased in dealing with theories of personality. One has the feeling that his long years of clinical experience have led him to avoid overemphasizing any particular aspects of the intra-organismal and interpersonal adjustments concerned in building and maintaining the person. A rather unusual accomplishment of this study is its maintenance of an ethical point of view without sacrifice of objectivity. The author stresses the importance, in dealing with the developing person, of arousing insight into not only the meaning of his reactions to the person himself but also their meaning for society. Realizing fully the difficulties involved, Dr. Healy still has faith in the possibilities of an educational program which will contribute to knowledge of self "fused into an emotionally tinged ideology."

Hérédité et Épilepsies. By L. Marchand. Price, 36 francs. Pp. 123. Paris: Nouvelle Revue Critique, 1938.

From about four hundred books and articles Marchand has made uncritical selection of data which bear on the subject of heredity in epilepsy. Although he has no statistical data of his own, he accepts from widely differing reports the statement that whereas the incidence of epilepsy in the general population is about 2 per thousand, among the descendants of epileptic persons it is 37 per thousand and among the ascendants 65 per thousand. He also presents the evidence of Rosanoff and of Conrad showing the high proportion of cases in which both similar twins are affected. In spite of this seemingly convincing evidence for heredity, the author concludes that not epilepsy, but only the cerebral pathologic state which causes epilepsy, is inherited. This he calls "paraheredity." Thus, heredosyphilis is responsible in 4 or 5 per cent of cases of epilepsy and causes a cerebral fragility which can be transmitted for several generations. Heredoalcoholism, defective fetal development and infections and intoxications of the mother, as well as obstetric traumatisms of the brain, all may cause epilepsy later in life.

In the opinion of the reviewer, the author trips over his assumption that heredity of a tendency to seizures and heredity of a cerebral pathologic condition are mutually exclusive. Marchand assumes that if a cerebral pathologic condition is present no constitutional tendency need or can be present. Apparently, he has overlooked the evidence of American authors that even patients with "symptomatic" or traumatic epilepsy have three times as many relatives with epilepsy as persons in the general population. He fails to realize that in a given person both constitutional predisposition and an acquired pathologic state may combine to produce seizures.

Further, Marchand argues that even if a "genotypical," inherent heredity of epilepsy existed, efforts at control by eugenic means would be useless because there is no means of detecting possible "carriers" of the epileptic predisposition. (The author in not aware that the electroencephalogram points out who among the "normal" relatives of epileptic persons are "carriers" of abnormal cortical rhythms.) Denying as he does the existence of true heredity, the author believes the only means of reducing the incidence of epilepsy is to combat syphilis and alcoholism, which reduce the vitality of germinal cells, to protect the mother against injuries to the embryo or to the infant at birth and to guard the growing child against any influence injurious to the brain.

Practical Neuroanatomy. A Textbook and Guide for the Study of the Form and Structure of the Nervous System. Adapted to the Needs of the Student and Practicing Physician. By J. H. Globus, M.D. Price, $6. Pp. 387, with 148 illustrations. Baltimore: William Wood & Company, 1937.

Dr. Globus presents the fundamentals of neuroanatomy (including the most important microscopic, physiologic and embryologic features) by guiding the student in his studies, step by step, from simple instructions how to handle a brain or cord to the methods of identifying individual structures (convolutions, sulci, blood vessels) by inspection, dissection and staining. Problems are offered for solution, with instructions to outline the observations on plates appended to the book. This method of teaching facilitates the understanding of the complex structure of the central nervous system, with its numerous tracts and masses of gray matter, their mutual relationship and their significance. The topographic features are always emphasized, and when individual sections, such as those of the medulla oblongata, are described, a detailed summary is given at the end of the chapter. The numerous splendid illustrations, with liberal legends, and a lucid style of writing render the reading easy and interesting. An altogether unusual feature is an outline of 16 cases of neurologic disorders which illustrate the clinical importance of some anatomic structures.

Clear and competent as the author's presentations are, there are occasional passages in the book which require elucidation and even correction. For instance, Holzer's crystal violet stain (page 166) is termed by the author "victoria blue stain"; "filum terminale" is spelled "filum terminalis"; the Argyll Robertson pupil is written with a hyphen; descriptions of the descending tracts of Schultze and Flechsig (oval field), given on pages 93 and 198, seem varied; the somewhat cursory description of the microglia—the "third element" of the central nervous system—is too concise and conveys an impression that it is a glial element.

With the exception of some obscure points, the book is well written, well arranged and splendidly printed. It is a unique contribution to neuroanatomy and should be of great value to any one who wishes to orient himself in the fundamentals of this basic medical science.

The Clinical Examination of the Nervous System. By G. H. Monrad-Krohn. Seventh Edition. Price, $3. Pp. 319, with 111 illustrations. New York: Paul B. Hoeber, Inc., 1938.

In its new, seventh edition this classic handbook on neurology has been extensively revised and enlarged. The new material includes additional illustrations, particularly in the chapter on ventriculography and encephalography, a short description of angiography and an outline of the examination of the unconscious patient. As in former editions, the book now includes a detailed and complete outline of the technic of neurologic examination. The psychiatric examination is also discussed briefly, and valuable chapters describe electrical examination, chronaximetry and chemical and cytologic examination of the cerebrospinal fluid. In an extensive appendix several miscellaneous subjects are discussed. There is a brief description of the Binet-Simon tests, as well as anatomic diagrams and sensory and motor charts. In his discussion of encephalography Monrad-Krohn describes the method of "small encephalography" proposed by Laruelle, in which a small amount of air (usually about 10 cc) is injected. By this method the penetration of air into the ventricular system demonstrates the absence of obstruction between the ventricles and the subarachnoid space, with little discomfort to the patient.

One cannot commend too highly this exceedingly valuable and still compact book. It is especially useful for beginners in clinical neurology, but has much to offer the more advanced neurologist.